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SKELETAL CHANGES RESEMBLING SCURVY IN INFANTILE HYPOTHYREOSIS BEFORE AND AFTER THYROID THERAPY[1]

by

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A number of papers from different countries have been devoted to the subject of roentgen skeletal changes in infantile hypothyreosis.

WILKINS, who has a comprehensive list of references, summarizes as the most important signs:

1. Delayed appearance of ossification centres.
2. Fragmented development of centres from multiple islands of ossification centres, which during growth form an irregular spongy, »fluffy» osseous structure.

These changes were observed in centres developed before any treatment had started and in centres, the appearance of which had been delayed, but appeared after treatment. The centres which appeared at normal time after the treatment had started, became ossified normally.

We have three patients with recently treated hypothyreosis where we also observed other changes.

The diagnosis of hypothyreosis has in our cases been established on the following basis:

1. Characteristic clinical signs.
2. Reduced longitudinal growth.
3. Mental debility.
4. Roentgen demonstration of delayed development of the ossification centres.
5. The effect of thyroid therapy.

[1] Submitted for publication, Oct. 3, 1950.

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Fig. 1. Case 1. 4 months old. Three ossification centres. (Normal according to ELGENMARK 8.5, standard deviation ± 2.8.) Fragmented structure of the femoral centre. Subsequently fragmented centre of the cuboid bone. Slight osteoporosis. Intensively saturated preparatory zone of calcification in long bones and round ossification centres. (The os calcis.)

The patients had a cretinoid appearance with myxoedematous skin and changes of the mucous membrane. The tongue was large, the voice rough and hoarse. The abdomen was enlarged, and all the patients had umbilical hernia. During treatment with thyroid extract the characteristic myxoedematous appearance gradually disappeared.

Case 1. V. K., ♀, serial number 3246 and 5525/1948. Born May 20, 1948. Weight at birth 3,050 grams. From birth she was limp and inert, with a large abdomen and constipation. Breast-fed the first few days, followed by artificial feeding, at first half-milk, then two-thirds milk. Addition of codliver oil and malt extract from the age of three months. No fruit juice before hospitalization. Poor appetite from birth — it had not been found possible to administer quantities of milk required for the age and weight. Admitted to hospital 1) September 28—October 21, 2) November 24—27, 1948. On first admission the weight was 4,310 grams, length 52 cm. From October 4, 1948 treated with thyroid extract (Tabl. Thyreoidea Nyco) first 0.10 g × 3, then 0.10 g × 1, and later these doses alternatingly every other day. Daily administration of fruit juice in addition to the routine infant diet. After discharge fruit or vegetables daily. On control on June 30, 1949, the weight was 8,430 grams, and the length 70 cm. Upon further control on March 4, 1950, weight 10 kilos and length 77.5 cm.

Roentgen examinations (Fig. 1, 2): These were carried out from the time of admission and subsequently with intervals of some months up to March 4, 1950. It appears from them that there has been considerably delayed development of ossification centres. At the age of four months she had 3 ossification centres, while according to ELGENMARK

Fig. 2. Case 1. 11 months old (after 7 months treatment). Satisfactory longitudinal growth, from 52 cm to 66.5 cm. Transverse lines in the tibia (linear) and in round ossification centres (os calcis annular). Outside the latter ring relatively normal dense bone surrounding a persistent osteoporotic centre corresponding to the size when thyroid therapy was commenced. Ossification centres have grown. Further centres appeared. Still considerably delayed development of centres for the age.

there should have been 8.5 with a standard deviation of $\pm$ 2.8. At the age of 21 months (after thyroid therapy for 17 months) she had 19 ossification centres. According to ELGENMARK there should normally have been 41.3 with a standard deviation of $\pm$ 8.6. A distinctly fragmented centre was visible when the cuboid bone began to appear after two months thyroid treatment.

We also noted a considerable number of *sutural bones* of the skull especially in the lambdoid region.

Further, as far as it is possible to judge there appears to be a general degree of osteoporosis present. The epiphyseal lines of the long bones and the peripheral margins of the ossification centres are well defined, with the presence of distinctly sharp lines and rings. Adjoining these lines corresponding linear rarefactions are seen in the metaphyses, annular in the ossification centres. Thus, in a round ossification centre three regions are observed, with varying structures: a central, relatively dense zone, on the outside of which there is a poorly calcified, well delimited ring, and outside this again a dense calcified zone forming a demarcation of the centre. We have observed that the dense preliminary zone of calcification persists after thyroid medication as a »transverse line» in the bones, while the longitudinal growth of the bones showed good development. In the round ossification centres the previous line of demarcation is seen to persist, while a ring of new osseous tissue grows outside it. A remarkably persistent central osteoporosis, contrasting with this ring of relatively dense bone is noted, and corresponds to the size of the centre before the patient received thyroid medication.

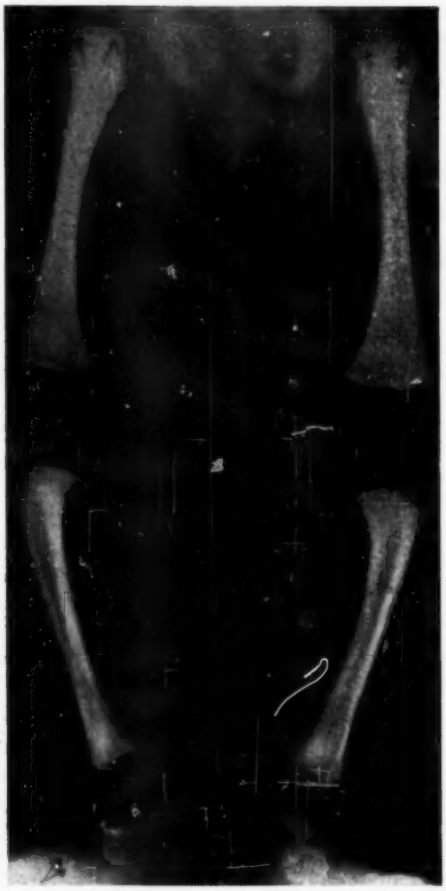

Fig. 3. Case 2. 5 months old. Length 55 cm. Roentgenogram from February 25: Fragmented centre for the cuboid bone (arrows). Irregular structure in the ossification centres of the knees. Centres for the talus and os calcis show centrally irregular, slightly osteoporotic structure surrounded by a rarefied zone around which there is a denser annular zone defining the centres.

Case 2. B. V. ♀. Serial number 8831/1949, born October 1, 1948, at full time. Not weighed. Non-thriving from birth with limp and inert appearance and poor appetite. Large abdomen. Breast-fed until admission. Hospitalized from February 22, to July 31, 1949. Weight on admission 4,600 grams. Length 55 cm. From March 2, 1949, treated with thyroid tablets (»Nyco») at first 0.10 g × 3 and subsequently 0.15 g × 1. Weight July 14, 1949, 7.4 kilos, length 66.5 cm.

Roentgen examinations from February 25 (Fig. 3) with intervals up to July 20, 1949. Thyroid therapy was commenced on March 2, 1949, with 0.10 g × 2, but has since varied between 0.15 × 1 and 0.10 g × 1.

Case 3. Th. R. ♀. Serial number 12022/49, born May 20, 1948. Weight at birth 3,875 grams. Breast-fed until admission. From the age of two weeks codliver oil, and from 4 months addition of malt extract and apples. No vegetables prior to admission. From birth she appeared flaccid and inert, had a large abdomen, was constipated, and had a poor appetite. Admitted from May to August 1949. Weight 7.3 kilos, length 62 cm. Treated with thyroid tablets, 0.10 g × 2 from May 19, 1949. Since discharge has had fruit or vegetables daily. Control in outpatient department October 10, 1949, weight 10.5 kilos, length 74 cm.

Roentgen examinations from May 16, 1949, to February 12, 1950.

Skeletal system examined by the method of ELGENMARK on May 16, 1949. Seven ossification centres found against normally 25.1 ± 8.7, thus a delayed development. The visible centres are small. Thus, the length of the os calcis is only 17 mm, and the osseous structure appears osteoporotic. Distinct »transverse lines» are seen a little distance from the shaft ends of the long bones. No distinctly fragmented centres appear, and as they are exceedingly small the osseous structure cannot be judged accurately.

Roentgen examination on July 20, 1949 showed that the centre in the proximal humeral epiphysis appeared fragmented. On October 12, 1949 the centres in the knee

Fig. 4. Same case, same age. Ossification centres of the femoral heads are absent. Metaphyseal rarefaction (»scurvy lines«?) in the femora with rarefied sickle-shaped lines (corresponding to the lines of growth) in the ilia, best seen on the right side (arrows).

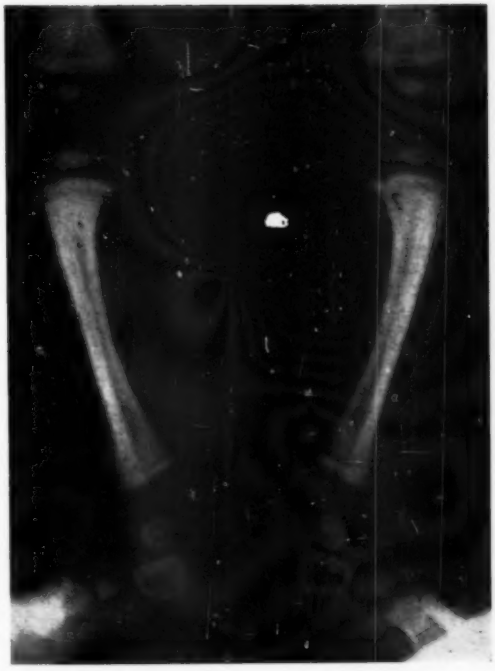

Fig. 5. Same case, 7 months old (after thyroid therapy). The cuboid centre on the right side has united, the left being distinctly fragmented. The zone of growth in the long bones and around ossification centres have increased and are denser, so that the persisting linear rarefactions in the metaphyses are more distinct. Corresponding annular rarefaction in the ossification centres. Increase in size of the centres of the knee satisfactory.

Fig. 6. Same case. 8 months old. Length 66 cm (after four months' thyroid therapy). Six ossification centres. (Normal according to ELGENMARK 14.6 ± 3.5, thus still delayed.) Satisfactory longitudinal growth. Transverse lines *e. g.* in the tibia, buried in the diaphysis (arrows) and around a persistent central osteoporosis *e. g.* in the os calcis. A ring of new dense bone around the calcaneum, indicating fairly satisfactory, perhaps normal growth. The centre of the cuboid bone no longer fragmented on any side.

region showed irregular structure, while the same centres had grown considerably on February 13, 1950. The distal femoral centre then was 23 mm wide and demonstrated a peripheral denser zone of calcification, indicating satisfactory growth, and otherwise, due to a slight central osteoporosis, resembled pictures found during the healing period in scurvy. On the same date the tibial transverse lines showed identical saturation and unchanged distance as when the thyroid therapy started. The length of the tibial shafts, however, had grown considerably.

After thyroid therapy from the age of 12 months to 21 months there are still only 19 ossification centres, while according to ELGENMARK she should have had 41.3 ± 8.6. We have, however, seen development of new centres which at first were fragmented, but subsequently becoming normal. The earliest sign of healing, however, seems to be the increasing length of the shafts of the long bones.

Due to the skeletal changes observed, which resemble scurvy, special laboratory tests were carried out in case 2 with a view to a possible complicating latent scurvy.

This was of all the more interest as the patient during the first 3 months after admission had received a diet of low ascorbic acid content, around 6 mg daily. By the end of the period three determinations of the

Fig. 7 and Fig. 8. Case 3. 12 and 14 months old. Roentgenograms from May 16 (left) and from July 20, after two months thyroid therapy. Arrows at the transverse lines show clearly how the shaft of the tibia has grown considerably. Peripheral dense zone of new bone around the os calcis. (The transverse lines never move.)

Fig. 9. Same case. Kyphotic angle between the first and second lumbal vertebra similar to the findings in the syndrome of Hurler. No signs of this disease in this case. Perhaps this finding may be seen in cases of hypothyreosis if we look for it.

fasting serum values of ascorbic acid were 0.0 mg per cent, 0.13 mg per cent, and 0.15 mg per cent respectively. The method used was the one prepared by BØE in 1946, and based on the reduction of methylene blue.

During the following period of 6 days the patient was given additional 70 mg ascorbic acid daily, corresponding to a supply of 10 mg per kilo bodyweight, the total quantity given fasting in the morning. The excretion of ascorbic acid in the urine was observed during the first five hours after the dosage. For this determination dichlorphenol-indophenol titration as described by HAGTVEDT (1940) was used.

The results of these investigations are tabulated below and show that there was no serious unsaturation at the time the test was commenced.

	Ascorbic acid excreted — percentage of amount administered.	Fasting values of ascorbic acid in serum.
1st test day.....	2.5 per cent	0.20 mg per cent
2nd » »	13.0 » »	
3rd » »	22.1 » »	0.54 » » »
4th » »	22.3 » »	
5th » »		
6th » »	42.4 » »	

In case 3 the serum ascorbic acid on May 16, 1949 was 0.71 mg per cent, on August 23, 1949, 1.4 mg per cent.

Comments

It should be stressed — as REYHER did as early as in 1912 — that the tarsi should be included in the roentgenological examination for the establishment of the diagnosis of hypothyreosis. The tarsus at birth already as a rule has three centres, viz. for the talus, the calcaneum and the cuboid bone, the latter in cases of hypothyreosis frequently being fragmented or absent. The tibial metaphyses are rapidly growing growth centres and will as a rule demonstrate disturbances in growth better and earlier than the metaphysis *e. g.* of the radius.

In our cases the roentgenological changes emphasized by WILKINS were present: Delayed appearance of ossification centres and fragmented development of centres. The numerous sutural bones in the skull, present in all three cases, seem to bear a relationship to the fragmentation of the centres. Additionally we noted a *dense* preparatory zone of calcification, linear in the metaphyses and annular around the round ossification centres. This was described by REYHER in 1912. Below these lines we observed a zone of rarefaction, as a rule a little thicker than the dense ones.

During thyroid therapy longitudinal growth and development of ossification centres occurred, while the previously mentioned two zones, the dense lines and the rarefied, persisted as tranverse lines (in the metaphyses) or annular (in the round centres). New bone was formed epiphyseally to the transverse lines of the long bones, and in the round ossification centres new bone was noted outside the dense annular rings, as a characteristic ring of probably normal bone. A persistent central osteoporosis in the round centres is seen in contrast to the dense peripheral bone ring (Fig. 2).

This kind of growth has generally been considered characteristic of scurvy in the stage of healing (WIMBERGER, PELKAN, MCLEAN and

McIntosh, Hotz). Wimberger states: »Thus the more or less wide marginal shadow surrounding the epiphyseal centres of the long bones is a specific sign of scurvy.»

We had in our cases, therefore, to consider the possibility of a concomitant scurvy. The clinical and laboratory data, however, did not procure evidence of ascorbic acid deficiency. In case 2 low serum values were found, but the saturation test did not show serious failing in saturation. In case 3 relatively high serum values, which would exclude active scurvy, were present.

It is known that the central osteoporosis associated with scurvy may persist for a very long time after treatment. The possibility, therefore, remains that the patients had gone through an active scorbutic period before they came under observation. According to the nutritional history, however, this theory seems improbable. We find it much more reasonable to consider these changes resembling scurvy to be part of the skeletal changes occurring in infantile hypothyreosis. The roentgenological similarity between scurvy and hypothyreosis under treatment seems to be easily explainable. We have active therapy for both these diseases and by its exhibition the condition of the patient is immediately changed from a pathological to a more normal metabolism, making the contrast between the diseased and normal osseous tissue marked and easily distinguishable. *The roentgenological examination hardly demonstrates characteristic changes per se, either in scurvy or hypothyreosis, but pathological osseous tissue in contrast to normal newly formed bone appears as a result of adequate therapy.* The fact that the pathological osseous tissue (for example central osteoporosis in the round centres) persists long after the actual bone growth has become normal, indicates that the normalization of old bone occurs more slowly than the growth of new bone in these regions.

The appearance of new centres is generally considered to be a sign of an effective therapy. In our experience increased longitudinal growth, clinically as well as roentgenologically, is an earlier sign of therapeutic effect. We have the impression that a higher dosage of thyroid is required for the development of centres than for the longitudinal growth.

The first effects of thyroid medication observed in our cases may be summarized as follows: Increased longitudinal growth with preparatory zones of calcification persisting as transverse lines in the long bones, in round centres a central persisting osteoporosis surrounded by a persisting annular density, and finally peripheral rings of newly formed bone of varying thickness proportional to the time period of therapy.

Such typical alteration may be observed after three to six weeks, and is in our experience a reliable criterion of the effect of the treatment.

SUMMARY

In three cases of infantile hypothyreosis the authors find the usual delayed development and fragmented irregular structure of ossification centres as well as arrested longitudinal growth. Numerous sutural bones seem to be associated with this condition. In one case there was a kyphotic angle between the 1st and 2nd lumbar vertebra.

Changes in the metaphyses and ossification centres, resembling those seen in scurvy, before and even after treatment, were noted. The reaction to effective treatment appears to be so definite after three to six weeks, that it may be of a certain importance in the therapeutical control.

ZUSAMMENFASSUNG

Bei 3 Fällen infantiler Hypothyreose stellen die Verfasser die übliche Verzögerung in der Entwicklung, die lückenhafte unregelmässige Struktur der Ossifikations-Centren und das gehemmte Längen-Wachstum fest. Zahlreiche Knochen-Nähte scheinen mitbeteiligt zu sein. In dem einen Falle fand sich eine kyphotische Winkel-Bildung zwischen dem 1. und 2. Lenden-Wirbel.

Es wurden Veränderungen an den Metaphysen und den Ossifikations-Centren, die denen glichen, wie man sie bei Skorbut beobachtet, vor und auch nach der Behandlung festgestellt. Die Reaktion auf eine wirksame Behandlung tritt nach 3 bis 6 Wochen so deutlich in Erscheinung, dass für die therapeutische Kontrolle dieser Tatsache eine gewisse Bedeutung zukommen mag.

RÉSUMÉ

Dans trois cas d'hypothyroïdie infantile les auteurs ont constaté le ralentissement ordinaire du développement ainsi que la structure fragmentaire et irrégulière des centres d'ossification suivis de l'arrêt de la croissance longitudinale. Plusieurs os suturaux semblent être intéressés par ces formations. Dans un cas il y avait un angle cyphotique entre la première et la seconde vertèbre lombaire.

Des altérations dans les métaphyses et dans les centres d'ossification rappelant ceux du scorbut, avant et même après le traitement, ont été constatées. La réaction due au traitement effectif semble être si appréciable après trois à six semaines que cela doit avoir une certaine importance pour le contrôle thérapeutique.

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DISCOGRAPHY OF DISSECTING TRANSOSSEOUS RUPTURES OF INTERVERTEBRAL DISCS IN THE LUMBAR REGION[1]

by

K. Lindblom

The earlier so-called »persisting epiphyses» (HANSON, JANKER, JOISTEN) or »persisting limbus vertebrae» (HELLMER) of the vertebral bodies (Figs. 1—2) are too well-known to be described here. The reason for the nomenclature was that they were thought to originate from the marginal epiphyses of the growing vertebral bodies. They have also been called

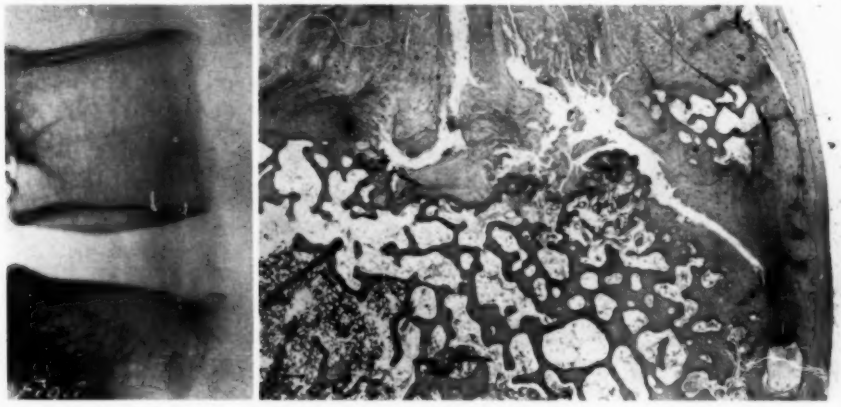

Fig. 1. Roentgenogram of an anatomical specimen with separated anterior margin of the fifth lumbar vertebra.

Fig. 2. Microphotograph of a sagittal section in the region of the separated margin in Fig. 1; the separation line has a fissure in communication with an anterior rupture in the intervertebral disc.

[1] Submitted for publication, March 15, 1951.

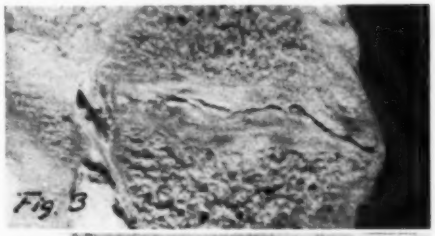

Fig. 3. Photograph of a sagittal section of a specimen with separated vertebral margin demonstrating disc rupture with a communicating fissure in the separation line.

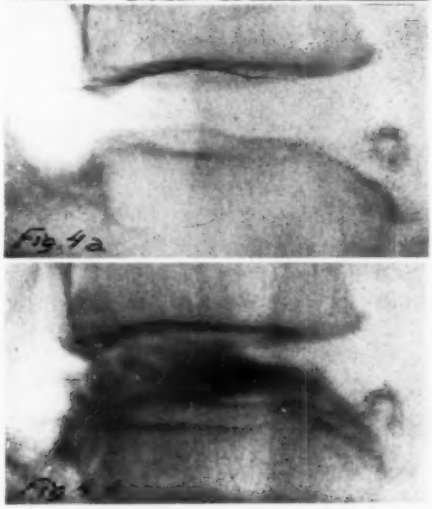

Fig. 4 a—b. Roentgenogram and discogram in a living subject demonstrating disc rupture dissecting through the anterior margin of the vertebra.

intercalary bones (SHANKS, KERLEY, TWINING). SCHMORL and JUNGHANNS, studying them in anatomical specimens, claimed that they were fragments of the vertebral margin which became separated by a long-standing protrusion of intervertebral disc tissue. They found disc tissue and fissures in the separation line.

»Persisting epiphyses» were studied by disc puncture and injection of dye into the disc centre (discography) in three anatomical specimens and in five living subjects. The dye spread through anterior disc ruptures into the »epiphyseal line» in all cases, thus demonstrating that this line is, in reality, a fissure, continuous with a disc rupture and dissecting anteriorly (Figs. 3—4).

So-called »persisting epiphyses» are usually situated anteriorly but may occasionally be found lying posteriorly. Such a case is illustrated in Fig. 5 a—b. A similar lesion found in an anatomical specimen is illustrated in Figs. 6—7. In this case a posterior disc rupture and herniation

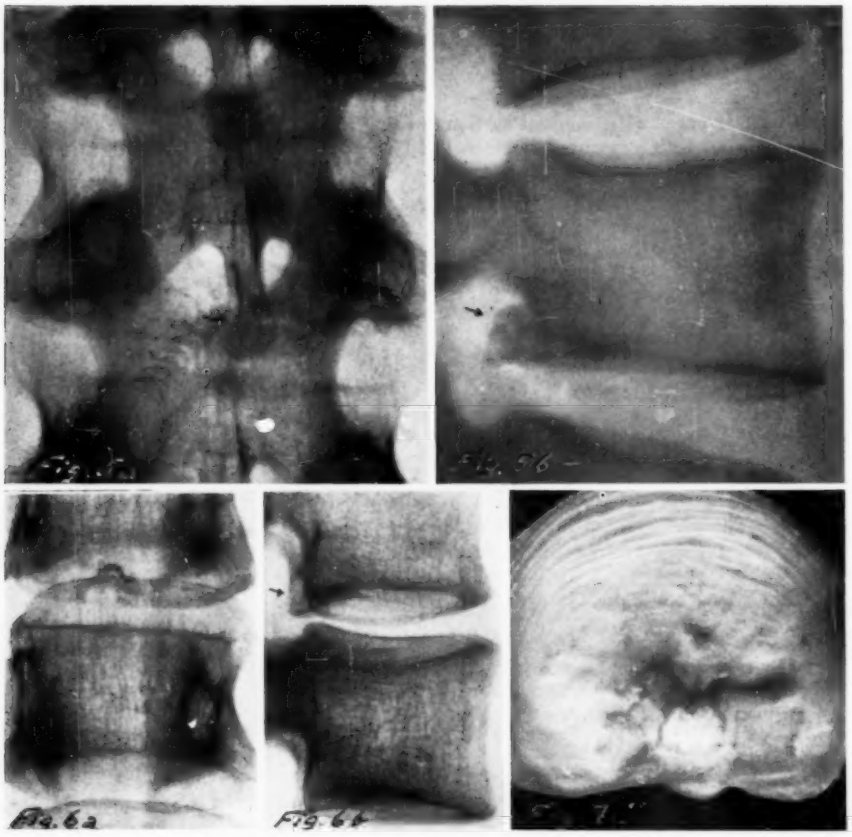

Fig. 5 a—b. Roentgenogram of a living subject with separated vertebral margin posteriorly. Arrows indicate the separation line.

Fig. 6 a—b. Roentgenograms of an anatomical specimen similar to the case in Fig. 5. Arrow indicates the separation line through which a posterior disc rupture and prolapse perforated the vertebral margin.

Fig. 7. Photograph of a horizontal section through the ruptured disc in Fig. 6. The disc is cut close to the vertebral surface where the disc prolapse is seen entering the bony canal and again appearing at the posterior surface of the disc.

had invaded the adjacent vertebra and continued through its posterior margin into the spinal canal, where a pea-sized prolapse was found. These cases must be considered as analogous to the above-described cases of anteriorly dissecting transosseous disc ruptures.

The clinical importance of vertebral »persisting epiphyses» is unknown.

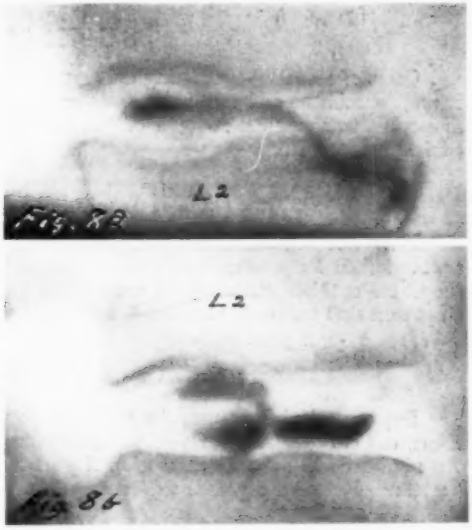

Fig. 8 a—b. Discograms in a living subject with a separated vertebral margin at the upper disc. The lower disc has an incomplete anterior rupture: the upper disc has an anteriorly perforating rupture continuing through the separation line, after which the dye spreads on out to the anterior surface of the vertebra causing abdominal pains. (See text.)

The injection of dye, however, into the anteriorly ruptured disc between L 1 and L 2 in the case illustrated in Fig. 8 a—b caused severe abdominal pain. A similar reaction on injection of anteriorly ruptured discs occurred in two other cases without »persisting epiphyses». It is therefore probable that anterior disc ruptures may be a cause of abdominal pains.[1] As the findings of anterior »persisting epiphyses» indicate anterior disc ruptures they may have clinical importance.

As regards the transosseous ruptures penetrating posteriorly there is no doubt that it is possible for the consecutive posterior bulging to produce symptoms by pressure on the posterior longitudinal ligament and the adjacent nervous structures.

Conclusions

So-called »persisting epiphyses» of the vertebral bodies are considered to be the result of dissecting transosseous ruptures of intervertebral discs. This concurs with the opinion of SCHMORL and JUNGHANNS.

Such dissecting transosseous ruptures occur anteriorly as well as posteriorly. They may cause clinical symptoms.

[1] In a paper by C. GRILL, Svenska Läkartidningen 1951: 399—403 (in Swedish), attention is directed to the possibility of abdominal pains arising from disc ruptures.

SUMMARY

Cases of so-called »persisting epiphyses» of vertebral bodies were examined in anatomical specimens and by discography in living subjects. The separation line contained dissecting transosseous rupture of the intervertebral disc. Such ruptures may cause clinical symptoms.

ZUSAMMENFASSUNG

Fälle mit sogenannten »persistierenden Epiphysen» der Wirbelkörper wurden in anatomischen Präparaten und durch Discographie bei Lebenden untersucht. Die Spaltungslinie enthielt dissezierende transossöse Ruptur der Zwischenwirbelscheibe. Solche Rupturen sind imstande klinische Symptome hervorrufen.

RÉSUMÉ

Des cas »d'épiphyse persistante» du corps vertébral, comme'on les nomme couramment, ont été examinés sur pièces anatomiques et par la discographie de sujets vivants. Au niveau de la ligne de séparation il y avait une faille transosseuse du disque intervertébral. De telles ruptures sont susceptibles de causer des symptômes cliniques.

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EXPERIENCES IN THE TREATMENT OF SKIN CANCER WITH ULTRASOFT ROENTGEN RAYS, 1933—1936[1]

by

Erik Ebbehøj

During the years 1933—36, 208 cases of cancer of the skin were treated with ultrasoft roentgen rays in the Radium Center for Jutland. None of these had received any previous treatment, and all diagnoses were microscopically verified.

At the same time 107 cases of chronic benign and doubtful ulcerations were subjected to treatment.

The benign and doubtful cases were treated in quite the same way and with the same doses as the malignant ones. As I had seen that the scars following this form of therapy were only slightly disfiguring, I had no hesitation about trying this uniform approach. None of the patients were hospitalized during the treatment. A biopsy specimen was taken, and then the lesion was curetted. When the bleeding had stopped, roentgen treatment was given to all the lesions. Two different qualities of rays were employed, adapted to the apparent thickness of the tumor.

Below I give an account of the 208 cases.

Of the 188 patients treated, 120 were men and 68 women; of these 17 patients had multiple cancers.

Microscopic Diagnosis.

Prickle-cell epithelioma	84	cases	(48	men,	27	women)
Basal-cell epithelioma	97	»	(55	»	35	»)
Epithelioma, unspecified type	26	»	(17	»	6	»)

Age Distribution of the 188 Patients.

	Prickle-cell	Basal-cell	Unspecified type	Epitheliomas
Under 20 years	0	0	1 (16 yrs)	1
20—30 »	2	1	0	3
30—40 »	2	5	0	7
40—50 »	7	8	1	16
50—60 »	14	20	1	35
60—70 »	24	26	12	62
70—80 »	17	18	6	41
80—90 »	9	12	2	23

[1] Aided by a grant from the Danish National Anti-Cancer League. Submitted for publication, Febr. 19, 1951.

Location.

Cheeks	65	Scalp	2
Nose	41	Neck	9
Lips	3	Body	7
Forehead	15	Thigh	1
Temples	19	Leg	3
Eyelid	15	Back of hand	11
Ears	17		

Thickness of the Epitheliomas.

	1 mm	1—2 mm	2—5 mm	> 5 mm	Not reported
Prickle-cell	18	16	26	13	11
Basal-cell	18	21	48	8	2
Unspecified type	6	9	9	3	
	42	46	83	24	13

Area.

Square mm.	< 50	50—100	100—500	500—1000	Not reported
Prickle-cell	16	20	33	7	8
Basal-cell	29	27	33	7	1
Unspecified type	4	2	13	6	2
	49	49	79	20	11

As will be seen from these tables, in Denmark skin cancers are not allowed to grow very large since medical aid is easily accessible and inexpensive to the patients. Still more important, there is a very comprehensive educational campaign, with lectures and pamphlets on cancer arranged by the National Anti-Cancer League. In these lectures and pamphlets people are instructed to consult their doctor if they develop persistent nodules or ulcers, even if the lesions are quite small. It is emphasized that, should a birthmark increase in size or begin to ulcerate, the patient must see a doctor at once.

To obtain a definite and cosmetically good therapeutic result in skin cancers it is indispensible that the tumor be small. The smaller it is, the better.

Treatment

All the 208 cases of skin cancer were treated with the same technique.

1. The ulcer and its vicinity are cleaned with alcohol. Iodine must not be used since it may absorb part of the soft roentgen rays and influence the effect.

2. No anesthetic is used. Particularly, infiltration anesthesia is not employed as it causes swelling and increases the thickness of the tumor, thus reducing the effect of the ultrasoft roentgen rays.

3. A small sample of tissue is taken for microscopic examination.

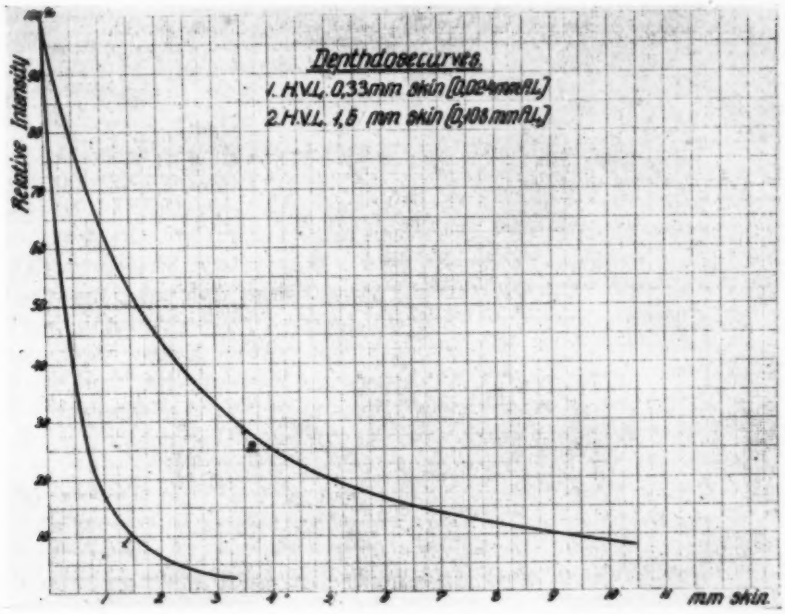

Fig. 1.

5. If it is not absolutely certain that the lesion is very superficial, less than 1 mm thick, it is scraped with a sharp curette.

5. A compression bandage is applied, with or without a non-metallic hemostatic agent.

6. Irradiation is not applied till oozing has stopped and the ulcer is dry. Even a thin layer of blood will absorb so much that the rays fail to penetrate deeply enough.

7. Tumors which after scraping are definitely less than 1 mm thick are irradiated with a quality of roentgen rays with H.V.L. 0.33 mm skin, produced by 12 kilovolts (fig. 1, curve 1).

If the lesion after scraping is estimated to be between 1 and 2 mm in thickness, a quality with H.V.L. 1.6 mm skin is used (fig. 1, curve 2).

Tumors which before scraping are estimated to be up to 2 mm thick are treated with the softer quality, while those which before scraping are over 2 mm in thickness are treated with the harder quality.

I want to emphasize that if the thickness of the tumor after scraping is more than 2 mm, it is necessary to use a harder quality or give a larger dose evaluated in accordance with the supposed thickness.

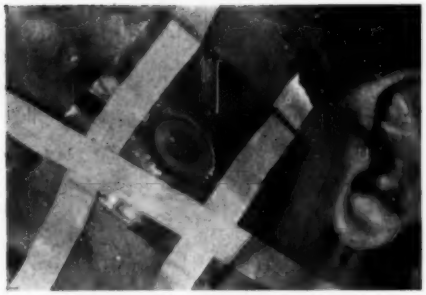

Fig. 2.

Fig. 3.

8. The ulcer is shielded with a screen of lead foil (1/3 mm thick), leaving 6 to 8 mm of normal skin exposed. The lead foil is fixed with adhesive plaster (fig. 2).

For eyelid cancer we use lead foil of a thickness of about 1 mm, with a hole for the tumor and a flap as illustrated (fig. 3).

After being covered with thin moist cellophane or rubber, the flap is inserted under the eyelid and bent in such a way that the tumor is pressed through the hole. In that way the tumor lies absolutely fixed and the eye is completely protected by lead (fig. 3).

Shields of the same type are used for cancer of the ear and lips.

9. The whole dose is given in one sitting of a few minutes' duration.

Reaction — Course — Scars

Erythema appears on the normal skin in the irradiated area on the day of treatment.

During the following 2—3 weeks an exudative radio-epidermitis develops (fig. 6). This heals in the course of 4—8 weeks. Small lesions will heal within 4 weeks after treatment, while larger ones will require about 8 weeks for involution.

Healing occurs most rapidly on the face and more slowly on the body and lower extremities. To facilitate healing of lesions in these latter areas it may be necessary to institute bed rest.

Treatment with the quality of roentgen rays with H.V.L. 0.33 mm skin leaves only a very slightly atrophic skin area, and the scar is often almost invisible. Depigmentation of the irradiated area often ensues. The scar becomes less visible with the years. Sometimes a small hyperpigmented zone may be caused by imperfect fitting of the lead-foil shield,

permitting some leakage at the edges of the irradiated zone. This pigmentation will fade in the course of 6—12 months.

Treatment with the quality H.V.L. 1.6 mm skin leaves a slightly more atrophic skin. Following the treatment a zone of skin around the irradiated area, about 2 mm wide, will very often show stretching of the follicular orifices due to shrinkage of the irradiated part, but generally it disappears after a couple of years.

Though inconspicuous, scars on the face are more readily visible after treatment with H.V.L. 1.6 mm skin than after H.V.L. 0.33 mm skin. This is the reason why I have employed both qualities in the roentgen treatment of skin cancers, although the former quality seems to be more constant in effect.

Results

In reporting the results of treatment of these 208 cases of skin cancer with ultrasoft roentgen rays, I have divided the cases into two groups, a small one of 34 cases and a larger of 174 cases.

When I started this treatment, I did not know so much about the depth-dose curves of these ultrasoft roentgen rays as I do now, and so the 34 cases were underdosed. After the lesions had been scraped, they received 8,000 to 15,000 r in one sitting with a quality of H.V.L. 0.33 mm skin, produced by 12 kilovolts.

At that time, I thought that this was an enormous dose. It was compared with dosages employed by other radiotherapeutists.

Accidentally, the first of these patients made good progress. Therefore it took some time before I realized that these doses were too small.

The results obtained in these 34 cases were bad. 3 did not heal at all, 1 recurred after 1 year, 4 after 2 years, 2 after 3 years, and 1 after 4 years. One patient did not report for follow-up examination. Twenty-two patients were free from recurrences after 5 years.

That is to say that in this group there were 11 failures among 34 cases, *i. e.* approximately 30 per cent, which must be considered a poor result.

The remaining 174 cases of skin cancer were given one of the following two dosages:

I: 20,000 r with a quality produced by 12 kilovolts in Bucky tubes and with H.V.L. 0.33 mm skin — amounting to a dosage of about 3,000 r at 1 mm depth, corresponding to about 1,000 r at 2 mm depth, and 500 r at 3 mm depth (fig. 1, curve 1).

II: 5,600 to 6,000 r with a quality produced by 26 kilovolts in a tube with a Lindemann window and an extra filter of 0.2 mm aluminium. H.V.L. 1.6 mm skin — amounting to 2,800—3,000 r at 1.6 mm depth,

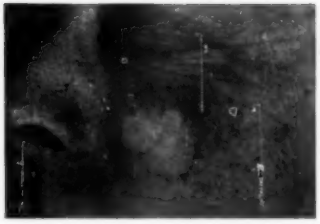

Fig. 4. Irradiated twice. H.V.L. 0.33 mm skin.

corresponding to about 2,500—2,700 r in 2 mm depth, and 1,800—1,900 r at 3 mm depth (fig. 1, curve 2).

These doses were given in one sitting in the course of 10—12 minutes.

Eight of these 174 cases of skin cancer were treated twice. Among these 8 patients there were 3 prickle-cell epitheliomas and 5 basal-cell epitheliomas; four were treated with 20,000 r H.V.L. 0.33 mm skin and the remaining four with 5,600 r H.V.L. 1.6 mm skin.

Reporting for inspection 2 months after treatment when the radio-reaction had healed, seven of these patients showed a little tumor tissue left over at the edge of the treated area, which had apparently not been large enough.

The remaining tumor tissue was treated again. All these patients were then free from recurrences for more than 5 years.

Fig. 4 shows one of these patients. The scar is rather conspicuous and disfiguring, but it has received double treatment in part of the area.

In one patient there was some cancer left over within the irradiated area after two months. The tumor was 4—5 mm thick. It was scraped

Table 1

174 Cases of Skin Cancer Treated with Ultrasoft Roentgen Rays

Epithelioma		Treated with		1 year			2 years			3 years			4 years			5 years		
		HVL .33	HVL 1.6	Fine	Dead	Unknown	Fine	Dead	Unknown	Fine	Dead	Unknown	Fine	Dead	Unknown	Fine	Dead	Unknown
Prickle-cell	70	35		32	1	2	+31	2	2	°30	2	2	30	2	2	°29	2	2
			35	+35			°34			34			33	1		33	1	
Basal-cell	82	33		32	1		30	3		°29	3		29	3		29	3	
			49	48		1	48		1	°47		1	45	2	1	44	3	1
Unspecified type	22	13		12		1	12		1	°10	1	1	8	3	1	8	3	1
			9	9			9			9			9			8	1	
Total	174	81	93	168	2	4	164	5	4	159	6	4	154	11	4	151	13	4
Recurrences° in previously involved area.	6 3.5 %	4 5 %	2 2 %					1			4						1	
Regional + metastases.	2	1	1		1			1										

and 20,000 r with H.V.L. 0.33 mm skin was applied. To avoid mistakes it should be remembered that if, before scraping, a tumor has a thickness of 2 mm or more, the H.V.L. 1.6 mm skin must be used. After a repeated treatment, this time with H.V.L. 1.6 mm skin, also this patient remained free from recurrence for more than 5 years.

Once again I want to emphasize that if the thickness of the tumor after scraping is more than 2 mm, it is necessary to use a harder quality or give a larger dose, evaluated in accordance with the supposed thickness.

Tumors infiltrating the deeper layers of the skin are obviously not suited for treatment with these soft qualities.

Metastases

Hematogenous metastases were not seen in these cases. Regional metastases appeared in 2 cases of prickle-cell epithelioma. In both cases metastases from the tumor appeared in a lymph node on the neck. The nodes were the size of walnuts. They were removed surgically, and the areas were treated intensively with hard roentgen rays; afterwards no recurrences for more than 5 years.

Recurrences

Cancer recurred locally in 6 cases.

One patient had a prickle-cell epithelioma of the ear, 5—6 mm thick adherent to the ear cartilage (fig. 5). After scraping, 5,600 r, H.V.L. 1.6 mm skin, was applied. Recurrence one year later (fig. 5). Amputation was done, and afterwards the patient remained well for more than 5 years.

I did this as an experiment, and it shows that deeply infiltrating cancer requires a greater dose or a harder quality.

In four patients cancer recurred two years after the treatment, the new lesions being in all cases located near the edge of the irradiated areas. One of these patients (prickle-cell epithelioma) was so old (82 years) and decrepit that she was unable to come for examination and treatment. Three were treated again. Two of these (basal-cell epithelioma) then remained

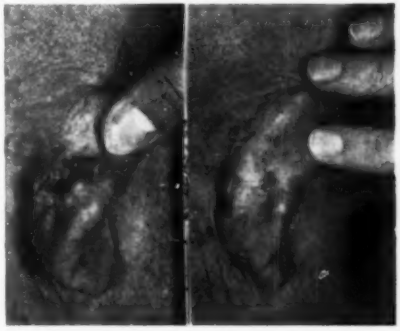

Fig. 5. Prickle-cell epithelioma treated with H.V.L. 1.6 mm skin, recurrence one year after irradiation.

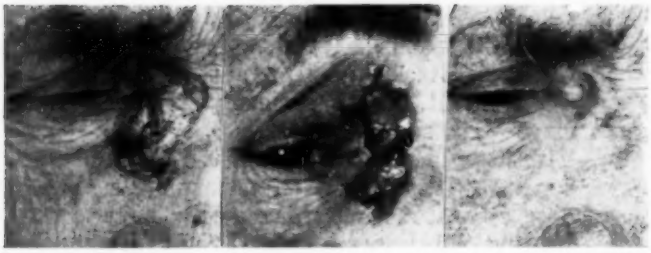

Fig. 6. Basal-cell epithelioma, treated with H.V.L. 1.6 mm skin, 3 weeks after treatment and about one year later.

Fig. 7 a.

Fig. 7 b.

Fig. 8 a.

Fig. 8 b.

Fig. 7 (above). Basal-cell epithelioma, treated with H.V.L. 1.6 mm skin.
Fig. 8. Prickle-cell epithelioma, treated with H.V.L. 1.6 mm skin.

well for more than 5 years; one (epithelioma, unspecified type) died 2 years later, 89 years old.

In one patient (prickle-cell epithelioma) recurrence appeared 4 years after treatment. It was treated again, but the following year the patient died of another illness.

Fig. 9. Prickle-cell epithelioma, treated with H.V.L. 1.6 mm skin.

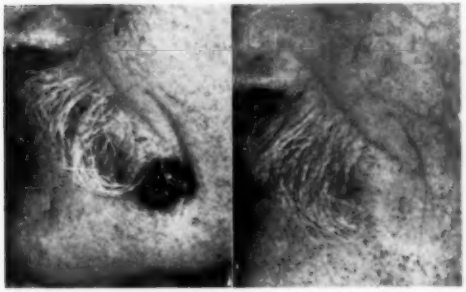

Fig. 10. Epithelioma, unspecified type, treated with H.V.L. 1.6 mm skin.

As will be seen, there were 6 recurrences among 174 cases of skin cancer treated according to these principles, *i. e.* 3.5 per cent. Four of these 6 recurrences were found among 81 cases treated with H.V.L. 0.33 mm skin and two among 93 treated with H.V.L. 1.6 mm skin. As has already been pointed out, the treatment with the quality of roentgen rays of H.V.L. 1.6 mm skin gives the most constant results.

Of these 6 cases three were free from recurrences for more than 5 years, two died 1—2 years after retreatment, and finally one was so weak that treatment had to be omitted.

Of the remaining 168 cases there were four of which we have no information. All these four patients had their cancer on the face. Two months after the treatment their lesions were healed, but since then I have not seen them.

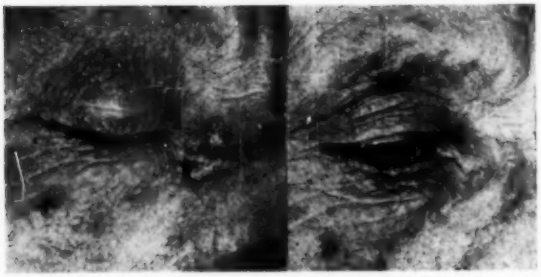

Fig. 11.
Basal-cell epithelioma, treated with H.V.L. 0.33 mm skin.

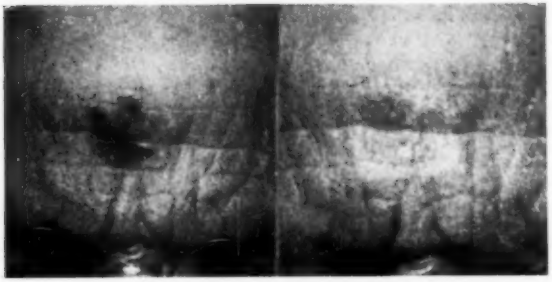

Fig. 12.
Prickle-cell epithelioma, treated with H.V.L. 0.33 mm skin.

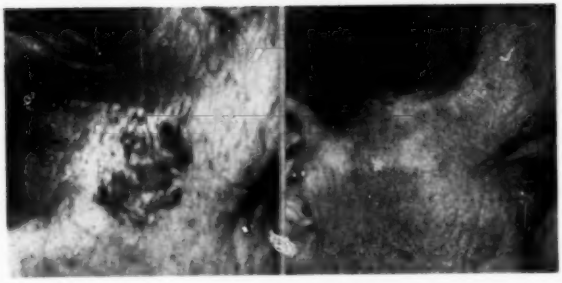

Fig. 13.
Prickle-cell epithelioma, treated with H.V.L. 0.33 mm skin.

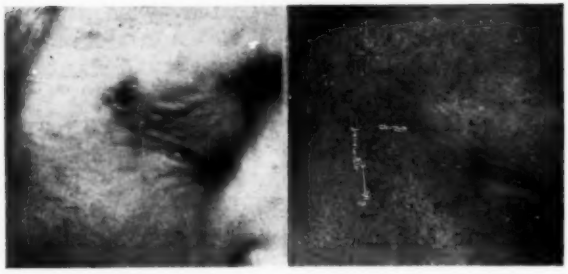

Fig. 14.
Epithelioma, unspecified type, treated with H.V.L. 0.33 mm skin.

The remaining 164 cases were free from recurrences for more than 5 years after treatment, or until they died of other illnesses. Thirteen patients died within 5 years.

A few photographs (figs. 6—14) showing typical skin cancers demonstrate the good cosmetic results of this form of irradiation.

SUMMARY

A brief account is given of the ultra-soft roentgen ray technique used in treating superficial cancers of the skin in which infiltration of the deeper layers has not occurred. The possibilities and limitations of this technique are discussed, and the results are reported.

ZUSAMMENFASSUNG

Es wird ein kurzer Bericht über die Verwendung ultra-weicher Röntgenstrahlen gegeben, die zur Behandlung oberflächlicher Haut-Carcinome benutzt werden, bei denen es zu einer Infiltration der tieferen Schichten noch nicht gekommen ist. Die Möglichkeiten und die Grenzen dieses Verfahrens werden besprochen und die Ergebnisse bekannt gegeben.

RÉSUMÉ

Une brève relation de la technique des rayons X ultra-mous appliqués au traitement des cancers superficiels de la peau dans lesquels il n'y a encore aucune infiltration des couches profondes. Les possibilités et les limites de cette technique sont discutées et les résultats relatés.

FROM THE RADIUM CENTER FOR JUTLAND, AARHUS, DENMARK.
(DIRECTOR: PROFESSOR CARL KREBS)

RESULTS OF TREATMENT OF SKIN CANCER WITH ULTRASOFT ROENTGEN RAYS GIVEN IN A SINGLE DOSE[1]

by

Eyvind Mosekilde

In the early thirties EBBEHØJ developed a method for the treatment of superficial skin lesions with ultrasoft roentgen rays. In his thesis he considered the physical properties of these rays in detail and in a paper (appearing in this issue) he reports on the procedure used in the treatment of skin cancers with these rays, the reaction of the tumor and the skin to this form of therapy, and his first experiences with regard to dosage, efficiency, etc.

Since 1936—37 this method has been employed as a routine treatment of small superficial skin cancers in the Radium Center for Jutland, and the five-year results obtained in such cancers treated during the years 1937—42 are reported in the following.

During these years 710 patients (432 men and 278 women) with skin cancer were treated. In these patients a total of 777 malignant epithelial tumors were encountered — melanosarcomas, sarcomas, cutaneous metastases, Paget's nipple disease, and cancers of the prolabium, the penis, the vulva, and at the anus being excluded. Thirty-one patients had two, four patients three, and two patients five cutaneous cancers.

The average age of the patients, when first seen, was 65.5 years. The age distribution, the distribution of the tumors according to site, and the histologic examinations were as could be expected in such a series.

Only such cases as had been histologically verified were included. In all 777 cases there was evidence of malignancy.

In order to obtain a fairly uniform material for the evaluation of this method of treatment only such cases as had not previously been sub-

[1] Submitted for publication, Febr. 19, 1951.

jected to treatment were included, since previously treated cases must be expected to have a more unfavourable prognosis. Only a comparatively small number, viz. 38, of the patients treated with ultrasoft rays had previously received treatment; in many of these the tumor had been removed surgically — sometimes shortly before the institution of irradiation therapy — so that the final result, whether successful or not, had to be attributed to the operation.

Among the 777 cancers there were *603 tumors in 556 patients which were exclusively treated with ultrasoft rays* (H. V. L. 1.6 mm skin) given in one sitting, *i. e.* approximately 85 per cent of all the patients with cutaneous cancer received this treatment. Information is available as to all but one of these patients.[1]

In addition, 39 clinical skin cancers, of which the histologic diagnoses were cancer(?), were treated with ultrasoft rays. After treatment with 26 kv., H. V. L. 1.6 mm skin, two recurrences were encountered among these patients, 2 and 5 years later, respectively; both recurrences disappeared after a renewed course of treatment. This group of patients was also excluded.

We considered the use of ultrasoft rays indicated when the tumor after scraping was between 1 and 2 mm in thickness, so that a sufficient amount of irradiation could be applied, also to the deeper layers of the tumor.

Factors of irradiation: A tube with a Lindemann window and an extra filter of 0.2 mm Al was used; 7 ma., distance 10 cm, H. V. L. 1.6 mm skin, 240 r/min. During the first two years (1937—38) most of the patients were given 5,100 r; a few received 6,000—7,000 r, and one 3,000 r. During the rest of the period under consideration most patients were given 4,200 r, a few received 5,000 r, and one patient, who had been given 2,600 r, died three years after the treatment without evidence of recurrence. All roentgen dosages refer to measurements in the air on the skin surface. Recurrences were not more frequent after 4,200 r than after 5,100 r. This may, perhaps, be due to the fact that during the latter part of the period we were inclined to scrape off a thicker layer of the tumor, so that a sufficient depth dose could be obtained, although this procedure may result in somewhat more conspicuous scars.

Primary Healing

In the treatment of the 603 skin cancers with ultrasoft rays, primary healing was accomplished in 582 cases or 96.8 per cent. By primary healing is understood that healing had occurred usually before the first fol-

[1] Only three patients received 12 kv., H. V. L. 0.33 mm skin; these patients were excluded.

low-up examination two months after the treatment; in a few cases it took, however, four months.

In the remaining 21 cases the course was as follows. In one case spontaneous healing occurred after one year; one case healed after treatment with Finsen light; in one case there was a small remainder at the first follow-up examination; the remainder was scraped off, whereafter the wound healed. Microscopy revealed chronic inflammation. In 11 cases a residual tumor was still left over at the first follow-up examination; healing was accomplished after renewed treatment. In one case the lesion did not heal until several courses of treatment had been given. In five cases the patients died before healing had been accomplished, and no information is available in one case.

Results

After an observation period of five years 394 patients with 420 cancers survived, while 162 patients with 183 cancers had died.

Of the 420 tumors 384 healed primarily and were permanently cured. In eight cases a small residual tumor was still present; it disappeared after renewed treatment without further recurrence. In 28 cases the cancer recurred. A survey is given in the following table.

	Treatment of recurrence	Result	Cases
One questionable recurrence	26 kv., H. V. L. 1.6 mm skin	Free from recurrences for the rest of the observation period	4
One recurrence	ditto		9
One recurrence	Short-distance therapy		4
One recurrence	Radium therapy		1
One recurrence	Operation		2
Two recurrences	26 kv., H. V. L. 1.6 mm skin		2
Two or more recurrences	Brief case histories reported below		6

Case Histories

No. 2196/38. Man, aged 68, first seen in November 1938. For 18 months an ulceration on the left side of the nose, extending to the adjacent part of the cheek (size 3 × 2 cm, not markedly infiltrated). Histologic diagnosis: basal-cell carcinoma. 5,100 r, 26 kv., were given. Primary healing within two months; then free from recurrence until the end of 1942. However, the patient did not present himself until May 1943, when a marginal recurrence, about 1.5 cm in diameter, had developed. Histologic diagnosis: basal-cell and prickle-cell carcinoma. 4,200 r, 26 kv., were given, and healing followed within two months. — Another pea-sized marginal recurrence in January 1947. Histologic diagnosis: basal-cell and prickle-cell carcinoma. Treatment: 500 r × 15, 60 kv., distance 3 cm. Primary healing within two months; yet a few crusts persisted; Finsen light gave some improvement. Since then no evidence of recurrence.

No. 159/38. Man, aged 66, first seen in January 1938. For 6 months a crust-covered lesion located to the upper part of the scapha of the left ear, 2 cm in diameter at the

first examination. Histologic diagnosis: solid carcinoma. Primary healing after 4,200 r, 26 kv. Nine months later (October 1938) a small recurrence. Histologic diagnosis: cancer(?). Treatment: 4,200 r, 26 kv. Healing within two months. In February 1941 a marginal ulceration, the size of half a pea. Histologic diagnosis: simple inflammation, but as it was cancer clinically, 4,200 r, 26 kv., were given. In spite of Finsen light the ulceration did not heal properly during the following year. In February 1942 a small residual tumor was observed. Histologic diagnosis: basal-cell carcinoma. Treatment: 500 r × 5, 60 kv. In July 1942 another recurrence or residual tumor. Histologic diagnosis: basal-cell carcinoma. Treatment: 500 r × 10, 60 kv. In September 1942 a residual tumor still persisted. Histologic diagnosis: basal-cell carcinoma. The ear was amputated, and since the patient has remained free from recurrences.

No. 1281/39. Man, aged 64; had received roentgen treatment 37 years previously for eczema on the back of both hands. The patient applied for treatment in June 1939. He had an ulceration, about 2.5 cm in diameter, at the base of the third finger of the left hand, which had developed after a blow on the hand two months previously. Microscopy revealed a cutaneous papilloma with chronic inflammation, but since clinically it was undoubtedly a cancer, 4,200 r, 26 kv., were given. The lesion did not heal properly but spread slightly. In August 1940 microscopic examination of a small marginal tumor showed solid carcinoma. The left hand was then amputated because of extensive marked changes in the skin.

No. 756/40. Man, aged 65, first seen in May 1940. He had an itching, oozing ulceration, measuring 5 × 3 cm, on the back, which had first been noticed two years previously. Histologic diagnosis: basal-cell carcinoma. Treatment: 4,200 r, 26 kv. From 1941 to August 1947 cancer recurred at the margin of the original lesion six times. Each time healing after 4,200 r, 26 kv. No recurrences since August 1947.

No. 1552/40. Woman, aged 58, applied for treatment in September 1940 with a lesion on the tip of her nose, which had persisted for 3—4 years. The ulceration, the size of half a pea, was surrounded by an elevated border, 0.5 cm wide. Histologic diagnosis: basal-cell carcinoma. Primary healing after 4,200 r, 26 kv. Recurrence, about 1.5 cm in diameter, in August 1943. Histologic diagnosis: basal-cell carcinoma. Treatment: 4,200 r, 26 kv. Although some crusts persisted, the lesion healed within two months. In November 1944 two marginal recurrences had developed. Histologic diagnosis: basal-cell carcinoma. Treatment: 4,200 r, 26 kv. Primary healing. Afterwards the patient complained of itching and incrustation in the nose, but no definite recurrence was encountered until in the autumn of 1946. On November 9, 1946, amputation of the nose was performed in the Radium Center of Copenhagen. Histologic examination revealed microcell carcinoma. Since then no recurrences.

No. 2569/42. Man, aged 57, had, when first seen in October 1942, a bean-sized tumor in the sulcus nasolabialis at the corner of the mouth, which had been present for 9 months. Histologic diagnosis: basal-cell carcinoma. Treatment: 4,200 r, 26 kv. In October 1943 a small marginal recurrence. Histologic diagnosis: basal-cell carcinoma. Treatment: 5,100 r, 26 kv. (owing to the thickness of the tumor). Primary healing. Recurrence in July 1944, appearing as a pea-sized cavity with infiltration, clinical cancer. No microscopic examination. Treatment: 1,000 r × 2 + 500 r × 11 = 7,500 r, 60 kv., distance 3 cm. Primary healing. Afterwards some occasional incrustation. In April 1946 some soft tissue at the upper edge. Histologic diagnosis: basal-cell carcinoma. Treatment: 4,200 r, 26 kv. In December 1946 a small marginal recurrence at the lower edge. Histologic diagnosis: basal-cell carcinoma ?. No treatment was given on account of the approaching Christmas. The wound has remained healed since January 1947.

Thus, among the patients surviving at the end of the five-year observation period the frequency of recurrence was 6.7 per cent, but 22 of the 28 recurring cancers were healed after renewed treatment, and the patients remained free from fresh recurrences for the rest of the observation period. Also the remaining 6 cases were free from recurrences at the end of the observation period, but had had essential discomfort from their lesions; in three cases resort had to be taken to amputation of ear, hand, and nose, respectively.

As previously pointed out, in the 162 patients, who died before the end of the observation period, 183 tumors were encountered. Of these, 163 healed primarily, and the patients died without evidence of recurrence. There was one case with a residual tumor, which healed after renewed treatment. Finally, there were 19 cases of cancer in 18 patients where the cancer recurred or the patient died from his cancer.

Recurrences

	Treatment of recurrence	Result	Cases
One recurrence	26 kv., H. V. L. 1.6 mm skin	Free from recurrences for the rest of the observation period.	3
One recurrence	Radium Treatment		1
Two recurrences	26 kv., H. V. L. 1.6 mm skin		2
Residual tumor and 3 recurrences	26 kv., H. V. L. 1.6 mm skin and short-distance therapy		1

Deaths from Tumor

Lymph node metastases and residual tumor at death	5 cases
Lymph node metastases, residual tumor healed at death	1 »
Lymph node metastases, tumor primarily healed at death and no local recurrence	5 »

No information available in one case.

Thus, the calculated percentage of cure becomes 90.4 since cancer recurred or death from cancer ensued in 47 of the 603 cases, and since, in addition, 11 recurrences could be expected among the patients who died from other causes before the end of the observation period (MAGNUSSON).

But the possibility of absence of recurrence after a five-year observation period reckoned from the first treatment with ultrasoft roentgen rays is approximately 97 per cent, provided that the patients are closely followed up and adequately treated for possible recurrences during this period.

About 94 per cent of the recurrences were encountered within the first 5 years.

Most frequently, the cause of recurrence was that the irradiated field

had been too small, since the majority of the recurring cancers appeared at the edge of the previously involved area. It is therefore very important to ensure that a sufficiently wide »free» zone is irradiated, *i. e.* 6—8 mm all the way round.

Furthermore, the size of the tumor plays a part, since it appeared that the percentage of recurrences increased with the diameter of the tumor; from 4—5 per cent in tumors less than 1 cm in diameter to 8—14 per cent in tumors with a diameter of 1—5 cm and 33 per cent in tumors with a diameter larger than 5 cm. An increase in the area involved is usually accompanied by a deeper infiltration.

On the other hand, the frequency of recurrence is independent of the age of the patient and the duration of symptoms. The recurrences seemed to be equally distributed among basal-cell and prickle-cell carcinomas, but a comparatively large number of deaths occurred among patients with prickle-cell carcinoma because of the greater tendency of this type of cancer to metastasize to the lymph nodes.

Unwanted Sequelae

There were only a comparatively small number of cases with unwanted sequelae, viz. 17, which were distributed as follows:

Slight incrustation	4 cases	
Ulceration (lasting a few months)	4 »	
Ulceration healed after Finsen light	3 »	
Slight ectropion	4 »	Distributed on 78 cases of carcinoma of the eyelid.
Epiphora	2 »	

Damage to the eyeball and its contents was not encountered.

Our method of treatment has proved extremely useful, and we intend to continue to carry it out on almost the same lines as described here. The treatment with ultrasoft rays saves time, and the patients need not necessarily be hospitalized. The latter point is of great importance in the treatment of cancers of the skin because the patients are often of advanced age and feel reluctant about being admitted to hospital, in some cases very far from their homes.

SUMMARY

Treatment of 603 cases of skin cancer with ultrasoft roentgen rays (H. V. L. 1.6 mm skin), given in one sitting, is reported. The calculated percentage of cure is 90.4. The method saves time and is very useful in the treatment of superficial cancers. Any recurrences encountered may be retreated successfully, so that the possibility of absence of recurrence after the five-year period is approximately 97 per cent.

ZUSAMMENFASSUNG

Bei 603 Fällen mit Hautkrebs wurde die Behandlung mit ultra-weichen Röntgenstrahlen (H. W. S.: 1.6 mm Haut.) in einer Behandlungs-Sitzung vorgenommen. Der Prozentsatz an Heilungen wurde mit 90.4 errechnet. Die Methode spart Zeit und ist durchaus nutzbringend bei den oberflächlich liegenden Carcinomen. Etwaig auftretende Rezidive können mit Erfolg wiederbehandelt werden, so dass nach Ablauf der 5-Jahres-Periode in annähernd 97 % Rezidiv-Freiheit besteht.

RÉSUMÉ

Le traitement de 603 cas de cancer de la peau par l'application de rayons Roentgen ultra-mous (pénétration 1.6 mm de peau) en une séance est décrit. Les guérisons sont de l'ordre de 90.4 %. La méthode économise du temps et est très appréciable dans le traitement des cancer superficiels. Les rechutes possibles peuvent être traitées à nouveau avec succès de façon que l'absence de rechute après cinq années d'observations est de 97 % des cas.

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THE ROENTGEN PICTURE IN CASES OF LUNG MYCOSIS[1]

by

Nils F. Bothén

Lung mycosis in the human being was described by different authors in medical literature as early as the eighteen-forties, but VIRCHOW was the first to give a scientifically acceptable description, when he published, in 1856, four cases of lung aspergillosis, determined by section. During the latter half of the nineteenth century, and at the beginning of the twentieth, further cases of lung mycosis were published, but it is only during the past twenty years or so that a larger number of such cases has been described, probably because of increased interest and wider possibilities of diagnosis during the patients' lifetime.

Among fungi which can give rise to lung mycoses, the yeast-like Monilia fungi are considered to take a prominent place. These are frequently present in all regions, even sometimes being found as saprophytes in the upper air passages of healthy individuals. A bronchopulmonary type of Monilia infection was described for the first time by CASTELLANI, in 1905, as being a disease found among tea-tasters in Ceylon. Since then cases have been reported from all parts of the world, and particularly from the tropics. Twenty cases of primary or secondary lung mycosis have hitherto been reported, more or less fully, in Sweden together with information as to the nature of the fungus found; eight of these were stated to be affections of mould-like fungi (Aspergillus and Mucor), while twelve were stated to be monilial infections. Of the latter cases, eight have been described by ERIK TÖRNELL, Borås, as so-called »thresher's lungs». The same author has also published eight cases of benign lymphogranulomatosis, where the presence of either yeast or mould fungi at the same time has been established.

[1] Read at the meeting of the Swedish Association for Medical Radiology, Stockholm, Nov. 25, 1950; submitted for publication, March 15, 1951.

Primary or secondary growth of fungus in the human lung does not seem to be such an unusual occurrence as was earlier believed. It has even been questioned latterly whether treatment with antibiotics, particularly aureomycin, may produce, at least in certain cases, favourable conditions for the growth of fungus in the lungs and elsewhere. Should this be the case, the possibility of a temporarily increased number of cases of lung mycosis must be reckoned with, a fact which is important for the roentgenologist to keep in mind at the present time when analysing obscure lung cases. It may therefore be of interest to show the roentgenological findings in three cases from St. Erik's Hospital, two of which have been defined as primary lung moniliasis.

Concerning the roentgenological changes in lung mycoses, it is sometimes pointed out that in the acute stages these resemble the changes in acute, unspecific infections such as bronchial pneumonia, while in chronic cases the changes simulate those in tuberculosis. Generally speaking, this is correct in most cases of lung mycosis, but a more detailed discussion of the subject may be of value. As the cases to be shown here concern lung moniliasis, the changes in this disease group will be primarily discussed; but, as American authors in particular have pointed out, the difference between the roentgenological findings in the various mycoses is so slight that it has not been possible hitherto to distinguish them with certainty from each other.

In mild cases of moniliasis, where only the bronchi are affected, no roentgenological changes, or only very small ones, are to be seen. These latter consist of insignificant peri-bronchial densities, with an occasional linear fibrosis. Usually, however, roentgen examinations in cases with greater or lesser degrees of changes show that the process often begins in the hilar regions, and spreads outwards along the bronchi and vessels within the lung parenchyma. The hilar shadows are often somewhat enlarged, but the enlargement is diffuse and marked lymph contours are usually not visible. The acute changes within the parenchyma ordinarily consist of small, smudged, patchlike densities, which have been described as looking like snowflakes, down, cottonwool and so on. The process may confine itself to one lung, but usually both lungs show changes. The lung-fields may then be strewn with such densities. The changes are chiefly localised to the middle and lower regions and are usually less marked at the apices. The densities can also become confluent, causing large dense areas. The pleura is sometimes involved, with exudation as a result. Cavities have also been described, but would appear to be unusual. With regard to the behaviour of the disease an occasional regression may often be encountered after some weeks or months, even without treatment. The roentgen picture may gradually become quite normal. In other cases the changes may develop into a more or less generalized

fibrosis, often with pictures simulating bronchiectasis. Such changes may remain as they are, or increase. It has also been stated that the disease may heal altogether, leaving disseminated calcifications. The roentgenological differential diagnosis of lung mycoses is very difficult, partly because of the variable roentgen picture, and partly because of its strong resemblance to other diseases of the lung. This is also the case with regard to lung moniliasis, where the changes are most like those in other lung mycoses, tuberculosis, benign lymphogranulomatosis, pneumonoconiosis, and carcinomatosis. In the acute stages of lung mycoses the inclination is to interpret the roentgenological changes as atypical pneumonia of unspecific variety. Miliary forms of non-specific lung infections and certain types of virus pneumonia may, for instance, be bewilderingly alike. It is obviously quite usual for both acute and chronic cases of primary lung mycosis to be diagnosed as miliary tuberculosis owing to the similarity of the roentgen pictures, but even confusion with other forms of tuberculosis may occur. As pointed out above, in cases of both lung moniliasis and other lung mycoses the parenchymal changes are for the most part confined to the middle and basal zones, while the apical areas show comparatively few changes, as opposed to lung tuberculosis, where the changes are primarily localised in the upper parts. Concerning benign lymphogranulomatosis, the question has been raised as to whether this is not actually a fungous disease, certain similarities indicating that this is the case. If, however, there is a suspicion of benign lymphogranulomatosis, a roentgen examination should be carried out, not only of the lungs but also of the bones of the hand, and even those of the foot. By this means changes typical of this disease may sometimes be observed. With regard to the differential diagnosis of silicosis it should be noted that in several forms of this disease group the changes are chiefly localised behind the hilus, which does not appear to be so in the lung mycoses. The roentgen pictures in cases of silicosis and mycosis are in other respects very similar.

Up to the present, it has been practically impossible in the majority of cases to distinguish the roentgen pictures in the different lung mycoses, and few roentgenologists have much experience in this field. In addition, opinions differ so widely that it is difficult to follow any standard rules. A study of the literature on the subject, however, shows that there are certain grounds for differential diagnosis, even though these are relatively uncertain. Thus it would seem, amongst other things, that miliary patches are relatively unusual in actinomycosis and aspergillosis, cavities relatively unusual in moniliasis and abscesses, and fistulae and pleural exudation very common in actinomycosis. These latter are not so common in other mycoses. Mixed infections of different fungi, such as aspergillosis and moniliasis, are also seen, thereby increasing the difficulty in diagnosis.

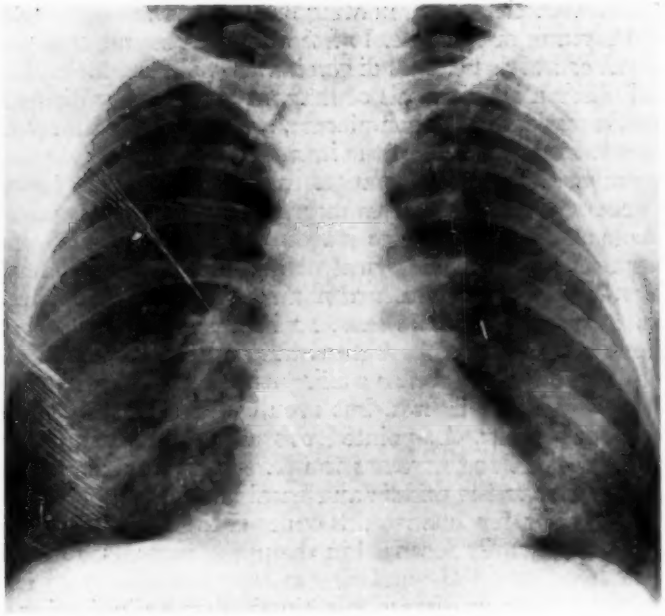


Fig. 1.

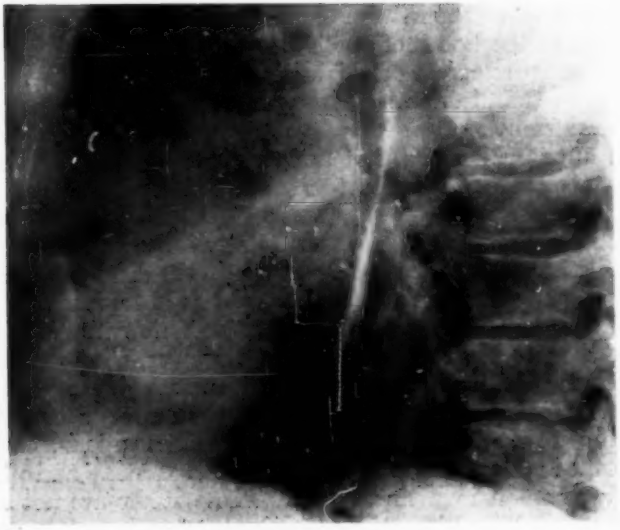
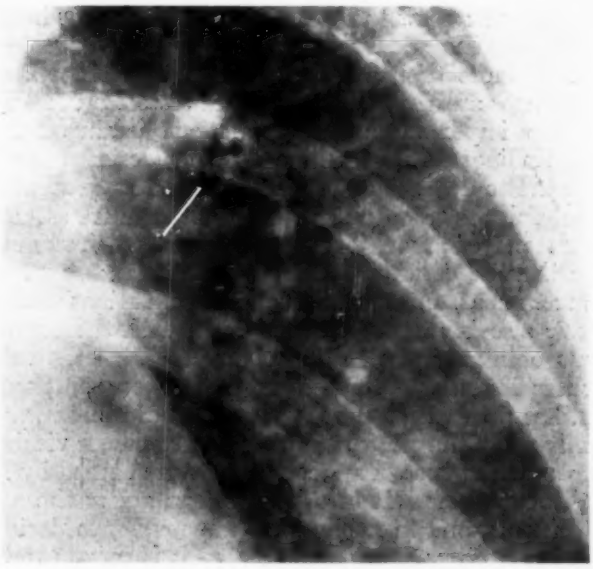


Fig. 2.

Fig. 1, 2 and 3. Case 1. March 1950. Widespread patchy opacities in both lungfields, most pronounced in the middle and basal regions. The hilar shadows are somewhat diffusely enlarged, showing no gland contours.

Fig. 3.



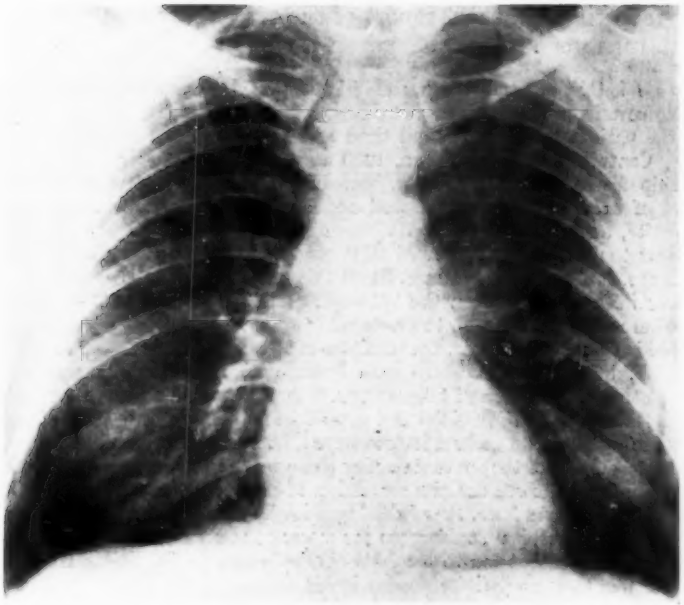


Fig. 4.

Fig. 4. Case 1. Oct. 1950. Regression of the lung changes, but a patchy increase of the lung shadows in the middle and basal regions, and a diffuse enlargement of the hilus shadows persists.

In spite of the fact that the most important findings in lung mycoses are made by roentgen examination of the lungs, the roentgen diagnosis itself cannot be more than a tentative one; this is because the roentgenological changes are far from typical and simulate those in other lung diseases. Of great importance in the diagnosis of lung mycosis, apart from the roentgen findings, is information in the individual case history regarding exposure to dust, the discovery of fungi by sputum culture, and even more helpful, the result of specimens obtained from the trachea and bronchi by means of bronchoscopy, as well as type examination of the fungus, investigation of its pathogeny and virulence, and the effect of the specific treatment. Intracutaneous tests, agglutination and precipitin reactions have also been tried in connection with the diagnosis of lung mycoses, but opinions are greatly divided regarding the value and reliability of these investigations. One of the pioneers of fungus diagnosis, CASTELLANI, has pointed out that the presence of fungi in the lungs does not necessarily mean that they are either pathogenic or virulent, and that they may be an occurrence of a secondary nature caused by lung changes of quite a different kind. Many other workers are of the same opinion. It is often difficult, and in many cases impossible, to decide whether a fungus infection is primary or secondary, as it is certain that changes in the lungs may be caused by both fungus and other lung diseases.

The following is a short report of the cases in question, dealing primarily with roentgenological changes in the lungs.

Case 1 is that of a policeman, aged 51, pensioned prematurely on grounds of dipsomania. No certain previous history of fungus or other lung disease. During the autumn of 1949 the patient was nervous and tired and had a cough. Roentgenogram at Stockholm City Central Dispensary in Jan. 1950 negative. At the beginning of Feb. 1950 the patient helped with threshing of oats, becoming in the middle of the same month tired and short of breath, with a cough and occasional blood streaks in the expectoration; poor appetite, and loss of weight. Roentgen examination at the Central Dispensary in Norrtälje at the end of Feb. showed widespread, small, round densities, chiefly basal, in both lungs. S.R. was then 71 mm. Since this date the patient has been twice treated at St. Erik's Hospital, between the 7/3—8/6, and between the 15/9—19/10, 1950. Repeated cultures of the sputum have produced fungus growth, proved by type examination to be Candida (Monilia) albicans. On admittance to the hospital in March 1950 the patient was feverish, but the temperature soon became normal. Mantoux was positive, but there were otherwise no signs of tuberculosis. The patient was treated first with penicillin and sulpha, later with gentian violet and potassium iodide. When discharged from hospital in July there was definite general improvement, both subjective and objective. S.R. was 26 mm. After culture of the sputum in May there was no fungus growth and the roentgen picture of the lungs showed definite regression of the changes, although patchy shadows, chiefly in the middle and lower lung fields, remained. After an overdose of sleeping draught the patient was in hospital at Långbro for a week in August, after which a cough, loss of appetite and diarrhoea led to his further admittance to St. Erik's Hospital in Sept. 1950. There was then no definite decline in his condition, and still further regressions of the lung changes could be observed roentgenologically, but culture of the sputum resulted in growth of Candida (Monilia) albicans.

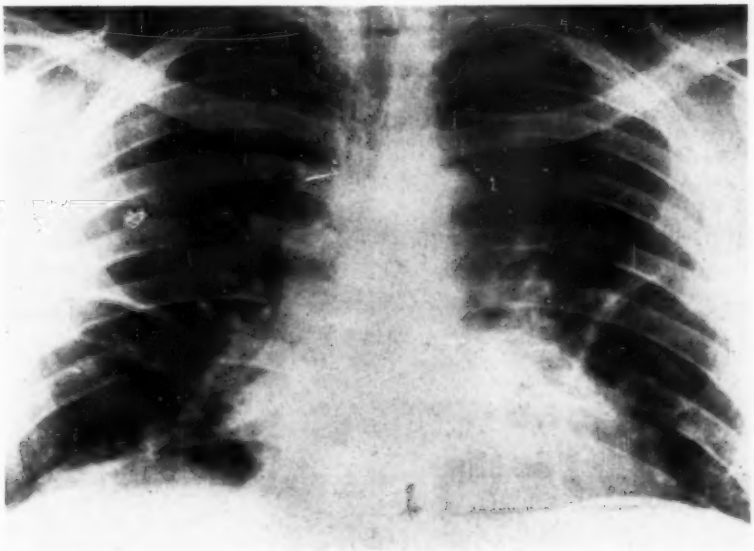


Fig. 5. Case 2. Sept. 1946. Both atelectatic-like, bandshaped densities, and relatively thin hazy opacities are seen in the middle and basal regions of both lungfields. The hilar shadows are diffusely enlarged and without gland contours.

The case may be summed up as being in all probability an example of recent, primary lung moniliasis in a 51-year-old man, contracted while helping with threshing. Grounds in favour of this diagnosis are as follows:

a) *The Roentgen picture.* Roentgenography, negative in Jan. 1950, showed extensive changes with the appearance and localisation common in lung moniliasis after the patient's threshing work in Feb.

b) *The finding of Candida albicans* after repeated cultures of the sputum. Absence of tubercle bacilli on repeated examination.

c) *The marked improvement after specific treatment.*

Case 2: A landowner, aged 50, who died at St. Erik's Hospital in August, 1949. According to information the patient had often taken part in threshing. Since about 1930 he had been troubled by shortness of breath and a dry cough, both of which increased during 1946. A roentgen examination was carried out in Sept. 1946, chiefly on account of heart trouble, and showed the latter to be somewhat enlarged. In addition, atelectasis and lesser infiltrations were observed basally in the lungfields on both sides, the changes being most marked on the right side. Roentgen control of the lungs after about two weeks showed slight regression of the basal infiltrations. In Dec. 1947 the patient was treated for pneumonia with sulpha, after which breathing became easier for a time. A gradual return and increase of symptoms, however, resulted in his admission

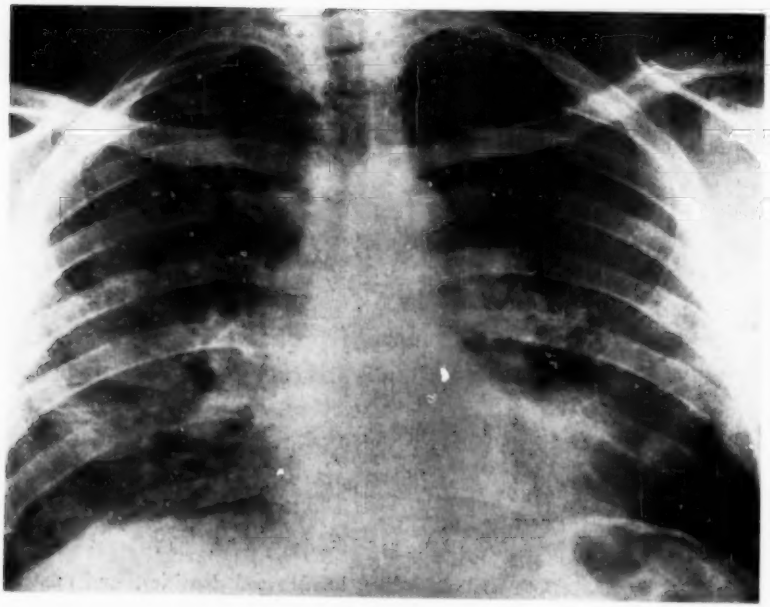


Fig. 6.

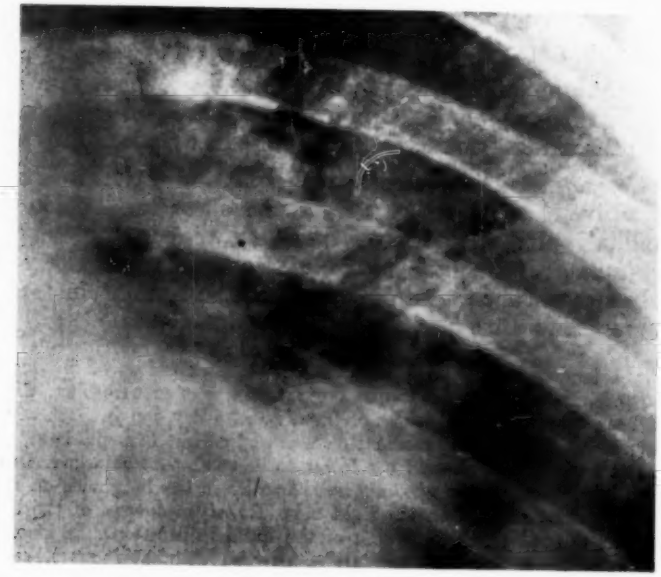


Fig. 7.

Fig. 6 and 7. Case 2. April 1949. Extremely widespread changes now in both lungfields, most pronounced in the lower two-thirds of the right and in the middle zone of the left lungfield. The changes consist, partly of a fibrotic streaky network, and partly of patchy opacities which are sometimes confluent. The hilar shadows are diffusely enlarged, dense and without gland contours. Local emphysema in the upper zones of the lungfields and at the left base.

to St. Erik's Hospital for the first time in Jan., 1948. The roentgen picture of the lungs showed little change since the autumn of 1946. S.R. was 35 mm. Hospital treatment during nine shorter and longer periods was continued from January 1948 onwards. In March 1948 a culture of the sputum made at the National Bacteriological Laboratory resulted for the first time in growth of a fungus, which type examination showed to be Monilia albicans. The same finding was made later by repeated control cultures. The patient was treated with, amongst other things, sulpha, penicillin, streptomycin, gentian violet and potassium iodide. Despite all care and treatment his condition gradually deteriorated. The roentgen picture was variable, showing periodical regression, but in the long run the changes increased and became more extensive, developing to some extent a fibrotic appearance. A large number of patchy opacities appeared, which were concentrated in the middle and basal parts of the lung fields, the hilus shadows showing a diffuse enlargement. Shortness of breath became more pronounced, finally increasing to an extreme air hunger, which necessitated the periodical use of oxygen with pressure.

At autopsy the lungs were exceedingly solid, compact and tough. Histologically, both lungs presented, in all lobes, a picture of almost homogeneous chronic pneumonia, with only a few scattered, aerated patches. Considerable fibrosis was visible both in the alveolar septa and the interstitial connective tissues, and there were also accumulations of thread-like, gram-positive mycelia, especially in the interstitial tissues. There were no signs of tuberculosis or a tumour. The mediastinal lymph glands were markedly hyperplastic, with signs of chronic lymphadenitis of unspecific character. The pathological diagnosis was Moniliasis pulmonum amborum in the form of chronic pneumonia. The heart showed considerable hypertrophy of both ventricles and very pronounced right-sided dilatation.

In summary the case is one of malignant, chronic lung moniliasis. The fungus infection may have been contracted while working at threshing. Grounds in favour of this diagnosis are as follows:

a) *The gradually increasing shortness of breath*, which is often a dominating symptom in lung mycosis, particularly in chronic cases.

b) *The roentgen picture*, with slowly progressing, chiefly patch-like and fibrotic changes, concentrated in the middle and basal parts, and the diffuse enlargement of the hilus shadows.

c) *The growth of Monilia albicans* as a result of repeated cultures of the sputum.

d) *The pathological diagnosis.*

Case 3. A 57-year-old woman, who died at St. Erik's Hospital in November, 1949. Lues about 1925, which was sporadically treated, the last time in 1947, when WR became negative. In 1930, probable dry pleurisy. Chronic polyarthritis since 1948, for which the patient received treatment at the Caroline Hospital. In May 1949, whilst there, she contracted left-sided bronchial pneumonia, and was treated with sulpha and penicillin. In spite of slow regression of the lung changes she remained feverish. In July 1949 infiltrations, simulating bronchial pneumonia, appeared at the base of the right lung, and sputum culture showed considerable growth of staphylococcus aureus. The patient was placed under private treatment, chiefly for the polyarthritis. In Oct. 1949 there was a rise in the temperature, and a roentgen examination showed a patchy increase of the lung shadows in the middle regions on both sides. The picture was suspicious of benign lymphogranulomatosis, but there were no other signs to indicate this disease. The patient received penicillin in dosage usual for pneumonia, but her temperature remained over

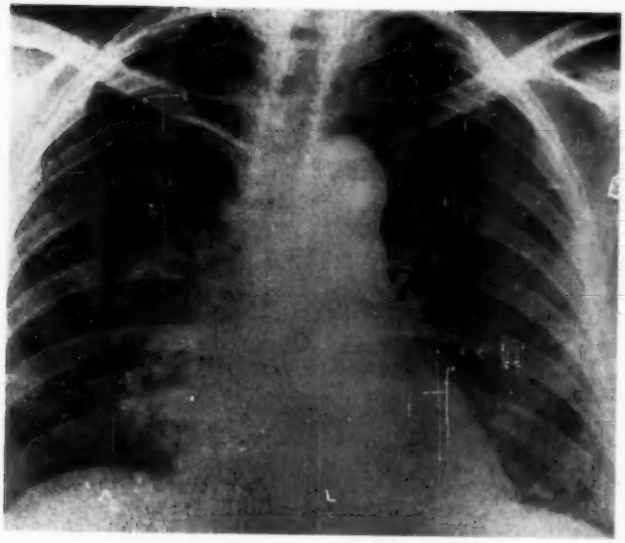


Fig. 8.

Fig. 9.

Fig. 8 and 9. Case 3. Oct. 1949. A network of streaky fibrotic changes with patchy increase of the lung shadows is situated in the lower two-thirds of both lungfields. No marked enlargement of the hilar shadows.

38° C. On admittance to St. Erik's Hospital on the 7/10 1949, she had had a temperature and a hacking cough without expectoration for five months, but was otherwise in fairly good condition. Roentgen examination of the lungs on 13/10 showed an increase of the central densities, but two weeks later there was a distinct regression. There were still, however, small spotlike and streaky shadows both in the middle and basal regions. The growth of Monilia was established in a culture of sputum, taken on 17/10. The patient gradually became more and more affected, grew somnolent, showed signs of heart inefficiency, and died of acute urine retention and uraemia in Nov. 1949.

Microscopic examination of parts of the lungs showed that the lung tissues were atelectatic in places, and small foci particularly in the peribronchial area were observed, simulating those of a chronic, almost completely healed, pneumonia. There was also a fairly diffuse growth of micro-organisms, the morphological appearance being consistent with Monilia. In one part of the bronchi micro-organisms of this kind had formed a colony the size of a pin's head. There were no signs of lues, tuberculosis or a tumour. The pathological diagnosis was Moniliasis pulmonum.

The case may be summed up as follows: The fairly intensive treatment of a 57-year-old woman for an infective disease, with lung changes simulating pneumonia, caused the arrest of this disease but also created conditions favourable for the growth of a fungus in the lungs; it is possible that this may have adversarily affected the prognosis. The pathological findings in this case were virtually diagnostic of mycosis. The fact that the culture of a single specimen of sputum, taken on the 17/10, produced growth of a fungus is of little importance. The early roentgenological changes were probably those of a non-specific pneumonia, but after some months' treatment with antibiotics, bilateral patchy shadows appeared in the mid- and basal zones, changes quite in keeping with an acute fungus infection. Later these changes assumed a more fibrotic appearance.

SUMMARY

Three cases of lung moniliasis are reported. The first is presented as a recent primary lung moniliasis, contracted by a patient while at work threshing, the second as a chronic, malignant lung moniliasis, while in the third, it is suggested that antibiotic treatment may have contributed to the development of a fungus infection. The roentgenologically demonstrable changes in lung mycoses are discussed, with special emphasis on the difficulties of differential diagnosis.

ZUSAMMENFASSUNG

Es wird über 3 Fälle mit Moniliasis der Lungen berichtet. Nach der Darstellung handelt es sich im ersten Falle um eine frische primäre Moniliasis der Lungen, die sich der Patient beim Dreschen zugezogen hat, im zweiten Fall um eine chronische maligne Moniliasis der Lungen, während im dritten Fall die Annahme besteht, dass eine antibiotische Behandlung zu der Entwicklung einer Pilz-Infektion beigetragen haben kann. Die röntgenologisch nachweisbaren Veränderungen bei der Lungen-Mykosis werden besprochen unter nachdrücklicher Betonung der bestehenden Schwierigkeiten bei der Differential-Diagnose.

RÉSUMÉ

Trois cas de moniliase pulmonaire sont relatés. Le premier est présenté comme un cas récent de moniliase primaire du poumon, contractée pendant une campagne de battage. Le second est un cas chronique de moniliase pulmonaire maligne, pendant que le troisième malade semble avoir acquis son infection mycotique au cours d'un traitement antibiotique. Les altérations de l'image radiologique dues à la mycose pulmonaire sont discutées avec considération spéciale de difficultés inhérentes au diagnostic.

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FROM THE ROENTGEN-DIAGNOSTIC DEPARTMENT (DIRECTOR: PROFESSOR OLLE OLSSON), UNIVERSITY CLINICS, LUND, SWEDEN.

STUDIES ON THE HEPATIC DUCTS IN CHOLANGIOGRAPHY

Suppl. LXXXIV, Acta Radiologica, 81 pages, 41 illustrations.

Autoreview

by

Olof Norman

The abundant literature on cholangiography contains but scanty reports on the diagnosis of stones or other pathologic conditions in the hepatic branches. Yet cholangiography during and after operation will visualize the intra-hepatic ducts just as well as it will the other sections of the bile ducts.

The nomenclature is defined and the technique used described. Intimate team work between the surgeon, radiologist, and anesthetist is vital for the production of satisfactory results. Owing to the topography of the hepatic branches films should be made at different angulations. Water soluble contrast medium is used.

The series examined was collected during the period 1. 1. 1947—30. 6. 50 from the Roentgen-Diagnostic Department and the Surgical Clinic of the University of Lund. Routine cholangiography visualized stones — verified later — in the hepatic branches in 46 of the patients examined during this period.

The description of the roentgen anatomy of the hepatic branches is based on C.-H. HJORTSJÖ's anatomical study of the hepatic tree. The morphological nature of cholangiography was exemplified by the demonstration of a large number of variants. Knowledge of the topography of the hepatic branches is necessary for discerning pathologic anomalies. Stones give the same signs in the hepatic branches as in other sections of the bile ducts.

Operative cholangiography is of practical importance for visualizing the anatomy of the ducts, particularly of ducts with an anomalous course. The nearer the ductus cysticus a duct empties, the more it is of surgical

interest, for it will then lie within the operative area and can easily be overlooked and injured.

Operative cholangiography is of greatest practical value for visualizing hepatic stones. Hepatic stones are usually accompaniments of choledocholithiasis but not infrequently of only a single calculus at the papilla. In a few of the cases an intra-hepatic stone was the only calculus observed in the deep bile ducts. But for cholangiography, these stones would have remained concealed. The importance of cholangiography was further illustrated by a few cases in which not all the stones were removed until control cholangiography at operation had revealed stones that would otherwise have been overlooked.

The differential diagnosis, which is practically the same as for other sections of the bile ducts, is exemplified.

Comparison of the cholangiograms and operative findings made at operation showed that about half of the hepatic stones could be removed, but that the other half were inaccessible to surgery. This new aspect is discussed with regard to the judgement of surgical results. The cause of postoperative distress is also elucidated by the fact that hepatic stones seem to be common, while the possibilities for the surgeon to remove them are limited. Re-examination of a series in which full use was made of cholangiography may also contribute to an elucidation of the question whether postoperative biliary distress is due to residual or newly-formed stones.

SUMMARY

The author gives a short abstract of his work »Studies on the Hepatic Ducts in Cholangiography» published as Supplementum 84 to Acta Radiologica.

ZUSAMMENFASSUNG

Verf. gibt eine kurze Zusammenfassung von seiner Arbeit »Studies on the Hepatic Ducts in Cholangiography» (Studien über die hepatischen Gallengänge bei Cholangiographie), veröffentlicht als Supplementum 84 der Acta Radiologica.

RÉSUMÉ

L'auteur donne une analyse abrégée de son ouvrage »Studies on the Hepatic Ducts in Cholangiography» (Étude sur les voies biliaires hépatiques par la cholangiographie), publié comme Supplementum 84 aux Acta Radiologica.

FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROFESSOR ERIK LINDGREN) AND THE MEDICAL CLINIC (DIRECTOR: PROFESSOR A. KRISTENSON) OF SERAFIMERLASARETTET, STOCKHOLM, SWEDEN

THE TREATMENT OF MULTIPLE MYELOMATA WITH RADIOACTIVE PHOSPHORUS[1]

by

E. Lindgren, I. Bergström and *G. Wihman*

Myelomatosis, a malignant disease running a course varying from several weeks to years, consists of a proliferation of abnormal plasma cells in the active bone-marrow. The replacement of the normal marrow provides the pre-requisite condition for anaemia, leucopenia and thrombopenia. Diffuse decalcification or multiple areas of destruction in the bones cause them to become brittle. A disturbance in the proportions of the albumen in the body is shown by the appearance of hyperglobulinemia and Bence Jones proteinuria. Skeletal pains and signs of severe renal damage as a rule dominate the usually complex picture which the disease presents. Many forms of treatment have been tried. Multiple myelomata are generally thought to be highly radiosensitive but GARLAND and KENNEDY have a somewhat different opinion. ANDA states that the »radioresponsiveness of the disease apparently varies». According to experiences we have had in the Roentgen Department of Serafimerlasarettet, roentgen treatment can in certain cases influence localised pain, but as the patient often has pain of a generalised character, or the site of the pain may vary from time to time, effective roentgen treatment presents certain difficulties. The course of the disease in its entirety seems, in our experience, to be hardly affected by roentgen treatment. This form of treatment would appear to us to be not of great value excepting in such cases in which pain is limited to a localised area of bone destruction. *Nitrogen mustard* appears to have no effect upon the disease. *Stilb-*

[1] Submitted for publication, April 10, 1951.

amidine, according to SNAPPER causes relief of pain and qualitative changes in the myeloma cells but has no definite effect upon the course of the disease and likewise no influence upon the radiological signs of skeletal changes. We have no experience ourselves of this method of treatment. *Antimony* may also be able to cause amelioration of pain (RUBINSTEIN). Up to now, *Urethane* has probably given the most encouraging results in producing freedom from pain, a return of the blood to normal and a decrease of the plasma cells in the bone marrow (LOGE and RUNDLES). The periods of observation are still relatively short. Some of the results of the treatment of various diseases of the blood with *Urethane* were presented at the Haematological Congress at Cambridge in 1950. It appeared from these that *Urethane*, during a sufficiently prolonged period, had proved disappointing. At the same time, the great disadvantages of the preparation *i. e.* gastro-intestinal reactions, the risk of aplastic anaemia, and necrosis of the liver, have been pointed out in various quarters. MOLONEY and HARRINGTON, presented a report at the Congress based upon twentyfive cases of myelomatosis treated with *Urethane*. In seven cases (28 %), a favourable effect on most of the symptoms was produced. One case developed necrosis of the liver. The acute forms on the whole did not react. The value of treatment with *Urethane* may thus be said to be still in dispute. HARRINGTON and MOLONEY consider, however, that *Urethane* should be tried out as »myelomatosis is a disease which has been persistently resistant to all forms of therapy».

Little has been written on the treatment of myelomatosis with radioactive phosphorus. DAMESHEK states in his 'Chemotherapy of leukaemia and leukosarcoma' that »RaP may be tried». J. H. LAWRENCE and his school are those who have had the greatest experience of the therapeutic use of radioactive phosphorus. LOW-BEER, LAWRENCE and STONE obtained varying results, freedom from pain and normal activity being secured in some cases, but there was no definite effect upon the roentgenological changes present. In their experience the results of treatment have not been uniform but have varied with the condition of the patient when the treatment was commenced. A 'marked relief of pain and a restoration to almost normal activity' has, however, been observed in several cases. No uniform technique of administration has been developed. In the one case in which dosage is mentioned, the patient is stated to have received 5 mC perorally and thereafter sixteen intravenous injections, spread over sixteen months, of a dose varying between 0.3 and 5.7 mC, with an average of 1 mC. BAYRD and HECK who published a summary based upon myelomatous material at the Mayo Clinic reported alleviation of pain in a small number of cases which had received RaP. Detailed studies of the bone marrow in association with the phosphorus treatment

do not appear to have been carried out. REINHARD, MOORE, BIERBAUM and MOORE have treated eight cases of myelomatosis with P^{32}. The results were summarized in the following manner: »Radioactive phosphorus has not proved to be a valuable therapeutic agent for the treatment of multiple myeloma.» Only one patient obtained relief from pain but the authors consider it doubtful whether it could be assigned to the phosphorus treatment. On the other hand they consider that the treatment, by bringing on leukopenia and thrombocytopenia, may shorten the expectation of life. The total dose in their cases varied between 5.0 and 17.7 mC. BAYRD and HALL have reported a case of acute myeloma which was treated with P^{32} (total dose 6.1 mC). The patient was restored to health after a short period, was free of signs about nine months afterwards, and had normal sternal bone marrow nine months from the onset of the first symptoms. They consider that this case signifies that P^{32} is not so valueless in the treatment of acute myeloma as the literature would suggest.

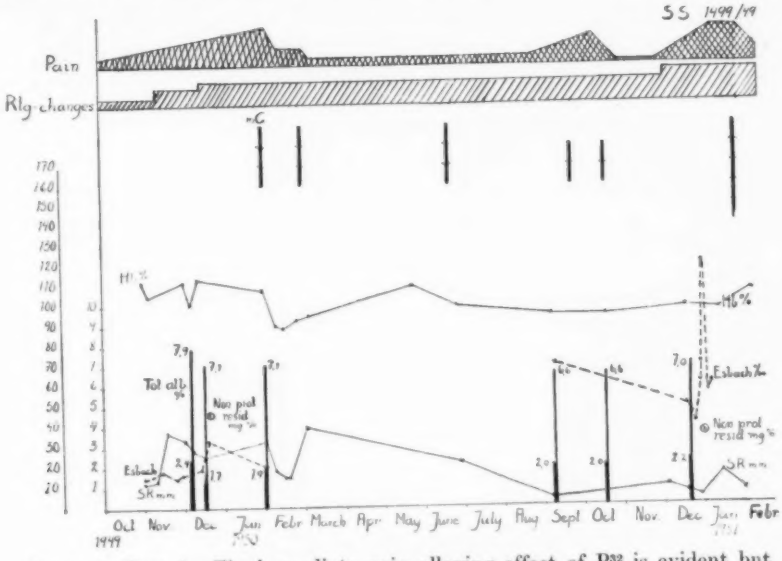
Some years ago, one of us tried phosphorus treatment on a female patient with wide-spread skeletal changes. She had previously been treated for several months in various ways, chiefly, however, with blood transfusions and roentgen therapy (but not with *Stilbamidine* or *Urethane*). When the treatment was commenced, the patient had been bedridden for several months with severe pain. The result of this trial treatment was most encouraging in as much as the patient became free from discomfort and was able to get up and look after herself fairly well for a period of about a year. By reason of the small number of favourable results which, on the whole, the previously used methods of treatment had given, and from the experience gained in this single case, we considered it reasonable to try out phosphorus treatment more systematically. This seemed to us to be desirable if only for the fact that the literature on the value of phosphorus treatment is relatively contradictory which is evident from what has been said above. Similar effects of pain relief noted in the case mentioned appear, however, to have been observed by others. Four further cases of myelomatosis have been treated since the first. Careful and repeated examinations of the bone marrow have been carried out in order to obtain a more accurate knowledge of the manner in which radioactive phosphorus acts and the eventual cell changes which occur. The material for the examination of the marrow has chiefly been obtained by sternal puncture but vertebral puncture has also been utilized. Both smear preparations and histological sections prepared according to a method which one of us (WIHMAN) has worked out, have been employed. In addition to a qualitative estimation, a differential estimation of the smear preparations, based upon 300 cells, has been carried out. We consider such a differential estimation justifiable in view of the

increasingly accepted view that myelomatosis is primarily not a localized hard and fast but rather a diffuse process of disease involving the whole of the bone marrow. In this connection, we would draw attention to, among others, RUBINSTEIN'S exposition of myelomatosis as a form of leukaemia. On those occasions when punctures have been made on various areas of bone marrow at the same time, no obvious variation in the composition of the marrow has been observed. Analogous with normal plasma cell series, myelomatous elements have been divided into three groups based upon their maturity: plasmablasts, proplasmacytes and plasmacytes. A note has also been made of multi-nuclear elements.

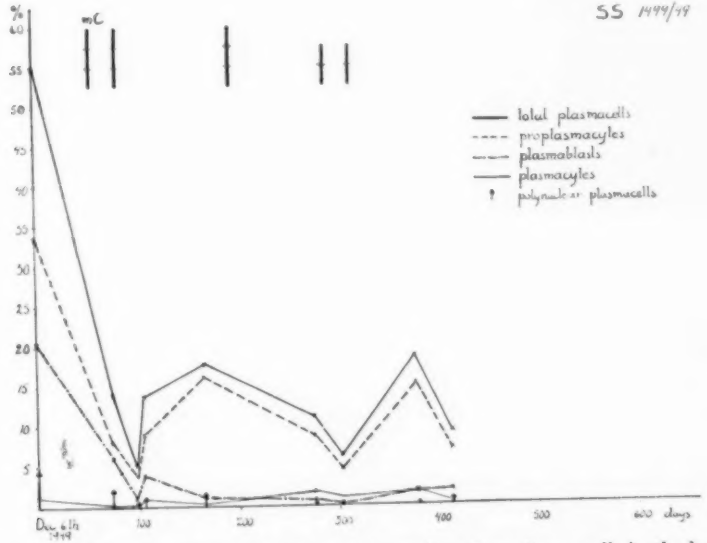
Radioactive phosphorus may be administered either orally or intravenously. The peroral method has been used in our cases as in our opinion this method is more easy to carry out: the demands of asepsis also disappear. As a result of a number of investigations (for example, by GREENBERG, COHN etc.) it has been shown that inorganic phosphorus is effectively absorbed from the digestive tract, and research both in animals and in man has suggested that at least 70 % of the amount ingested is assimilated if administered on an empty stomach. LAWRENCE, TUTTLE and SCOTT have demonstrated in animals that absorption is improved if P^{32} be given in solution with glucose. On the other hand, there are certain experimental data which suggest that the preparation is utilised somewhat better by the body when injected intravenously than when administered by mouth. When phosphorus is injected into the venous system, some 25 % is discarded by the body however during the first twenty-four hours and is chiefly excreted in the urine. After that the excretion diminishes rapidly and by the end of three days becomes less than 1 %. The patients in our series have all been given a tumbler of 10 % glucose solution containing the P^{32} to drink in the morning upon an empty stomach. The phosphorus has been administered in the form of Na_2HPO_4. The dosage, varying between 1.5 and 4 mC, is given in the text accompanying the curves. In the experience of one of us (LINDGREN) of the treatment of leukaemia and polycythemia, the therapeutic effects which have been observed when the drug has been given by mouth have not obviously been very different from those obtained by its intravenous administration.

Case Reports

Case 1. S. S. ♂ Aged 55. (Curves 1 and 2.) Warded April 1949 for suspected renal tuberculosis. He had then old healed t.b. changes in the lungs. The diagnosis of renal tuberculosis could not be confirmed. He was then admitted here in October 1949 for the investigation of general symptoms, particularly lassitude and pain in the chest. Changes of bone structure in several ribs were noted during a roentgen examination of the lungs.



Curve 1. Case 1. The immediate pain allaying effect of P^{32} is evident but the curves show no other changes in the existing conditions.



Curve 2. Case 1. Decrease in the total number of myeloma cells in the bone marrow. Above all a decrease in the immature and multi-nuclear plasma cells.

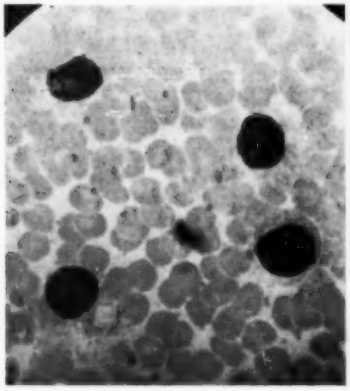


Fig. 1.

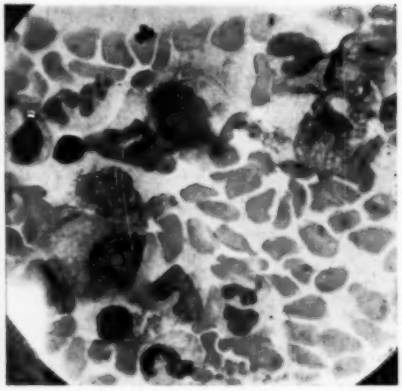


Fig. 2.

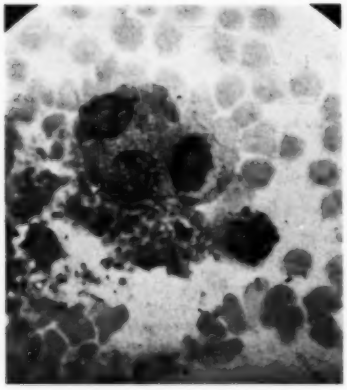


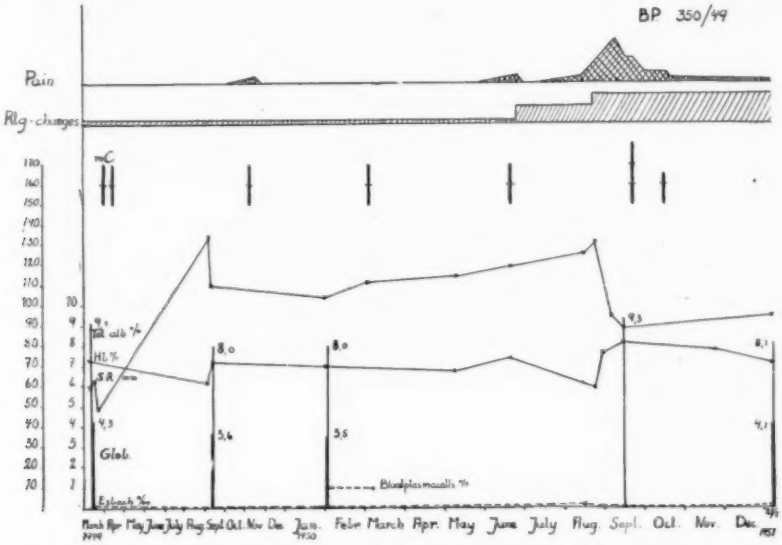
Fig. 3.

Fig. 1. (Case 1. Magn. × 560.) Smear preparation before P^{32} treatment. Myeloma cells of malignant appearance with giant nucleoli. Chromatin structure corresponding to proplasmacytes. Homogeneous protoplasma.

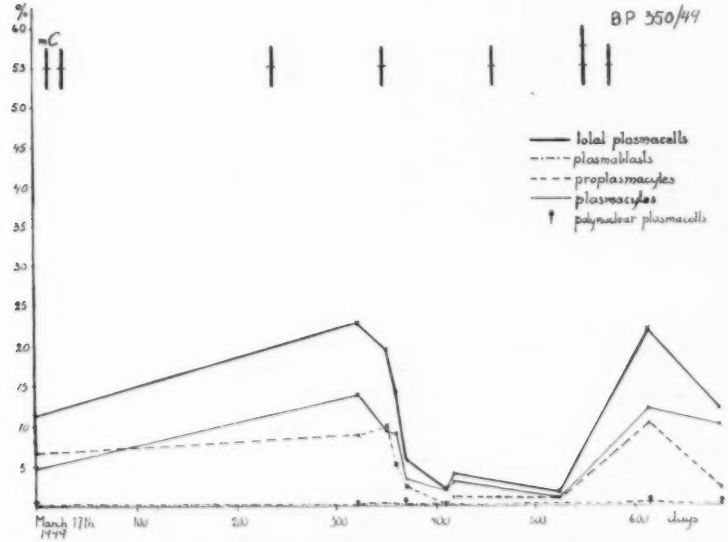
Fig. 2. (Case 1. Magn. × 560.) Smear preparation from same patient after treatment. Obvious qualitative changes in the myeloma cells. The chromatin structure is broken-up and disintegrated. The nucleoli are irregular. The normal marrow elements are without changes.

Fig. 3. (Case 1. Magn. × 560.) Smear preparation. Multinuclear myeloma cell showing the effects of phosphorus. The chromatin lies in coarse broken rods. The nucleoli are irregular.

The changes had been also observed upon a previous hospital visit but had then appeared to be in the nature of tuberculous osteitis. The appearances of the process of bone destruction now seen made this diagnosis however less probable. A specimen excised from an area of change in a rib revealed tumour tissue formed solely of plasma cells. *Sternal puncture:* Ordinary cell count. Picture dominated by plasma cellular elements which form 40—60 % of all the nucleated cells. These have a dysplastic appearance and are conspicuously uniform, immature and for the most part furnished with a very large nucleolus. Normoblastic erythropoiesis, displaced. No megakaryocytes. Total albumen and globulin estimation was, in the main, normal. S. R. 13. Esbach 1.5. Non protein nitrogen 46. Phosphorus treatment was carried out in January 1950 when the diagnosis was then clear. The dosage is given in curve 1. Considerable relief of pain occurred quickly after every dose of phosphorus. The sedimentation rate fell. The total albumen and globulin



Curve 3. Case 2. The pain allaying effect is apparent, but the curves show no other changes in the existing conditions.



Curve 4. Case 2. Distribution and total number of myeloma cells in the bone marrow during phosphorus treatment.

estimation on the other hand remained unaltered and the skeletal changes progressed during the period of observation. *Examinations of the bone marrow* showed marked and interesting changes. The number of plasma cells had become fewer in number. This held good especially for the immature elements, the plasmablasts and proplasma cells, but the multi-nuclear elements had also decreased in number. The greatest decrease in the number of plasma cells occurred after the first two consecutive doses of phosphorus. The picture remained fairly stable over a period of a year from then with a predomination of plasma cells while the malignant plasmablasts disappeared. Qualitative changes in the myeloma cells also took place after the phosphorus treatment. These qualitative changes have consisted of the appearance of bizarre, angular and irregular nucleoli, changed chromatinic structure with segmentation of the chromatin bars. These qualitative changes in these particular cells have still been apparent a long time after the phosphorus treatment. Normal bone marrow elements showed no changes either from a qualitative or quantitative aspect. The microscopical appearances as seen in histological specimens were those of a moderate degree of hyperplasia of the marrow rods with some reduction in the number of fat cells.

Case 2. B. P. ♂ Aged 57. (Curves 3 and 4.) Pneumonia 1947. Had then a S. R. of 120 which when checked later had not fallen to any extent. In 1949, patient came up to the Serafimerlasarett complaining of lassitude. Small punched-out areas, as seen in

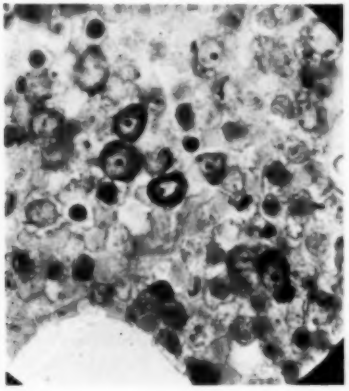


Fig. 4. (Case 2. Magn. × 560.) Microscopic section before treatment with P^{32}. Diffuse proliferation of myelomatous elements in the marrow bars with marked basophile protoplasm and a round giant nucleolus suggesting malignancy.

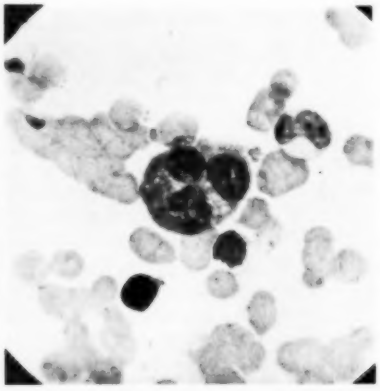
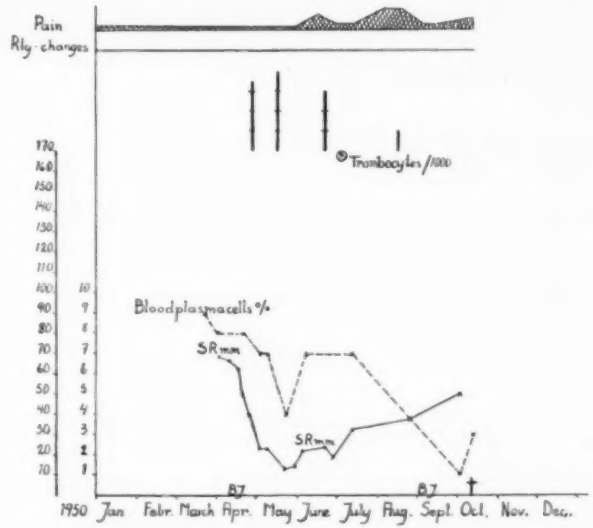
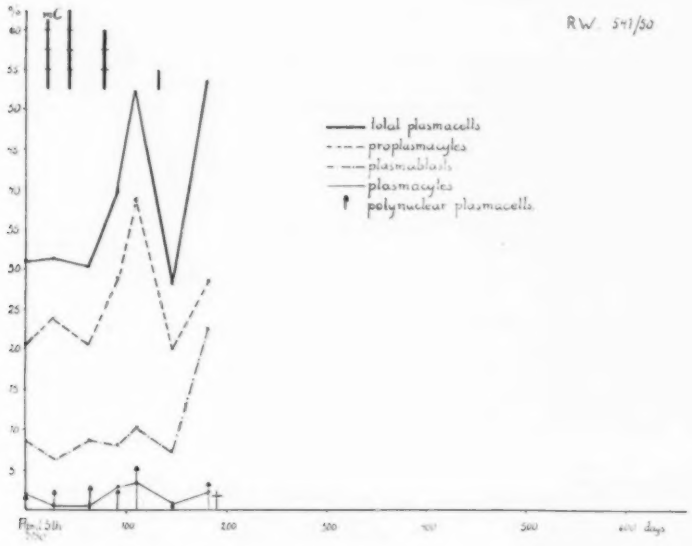


Fig. 5. (Case 2. Magn. × 600.) Smear preparation. A multi-nuclear myeloma cell after treatment. The chromatin lies in coarse sparse rods. The nucleoli are irregular. The cytoplasm contains a large amount vacuoles.

myelomatosis, were noted on roentgen examination. *Sternal puncture:* smear preparation: ordinary cell relationship. Myelo-erythropoiesis fraction 4 : 1. Normaloblastic erythropoiesis without any special characteristics. Myelopoiesis moved over slightly to the left. Abundance of plasma cells of different degrees of maturity, about 10 %. These also



Curve 5. Case 3. The number of plasma cells in the blood and the S. R. fell during phosphorus treatment. The effect of the relief of pain is evident but not to such a marked extent as in Case 2.



Curve 6. Case 3. No quantitative effect upon the bone marrow.

showed qualitative changes with increased vacuolisation and cell anomalities. No extracellular plasma cell bodies present. Few megakaryocytes noted. Histological preparation: an increase in the plasma cellular elements were also found in the sections. Appearances completely characteristic of myelomatosis were, however, not observed. S. R. 63. Total albumen 9.1. Globulin 4.3. Esbach 0.1. Phosphorus treatment commenced 1 April 1949. About six months later, in September, the patient complained of slight (described as »like a band» ♀) pain, in the chest, and was given a further dose of phosphorus (see curve 3). The pain then completely vanished. Extremely severe pain arose during the period but was relieved or completely removed in a short time by phosphorus medication. The roentgenological changes in the skeleton, however, progressed. The S. R., total albumen and globulin index remained raised the whole time and did not vary noticeably. The haemoglobin % was unchanged around 70. Repeated *examinations of the bone marrow* were first carried out ten months after the first, and three months after the third treatment. The plasma cellular elements then amounted to 23 % of which 13.5 % were plasmacytes and 8.5 % proplasmacytes. Repeated examinations were made after the fourth treatment with phosphorus and a rapid decrease in the number both of proplasma cells and plasmacytes was observed. The total number of plasma cell elements went down to 2.3 %, most of these now consisting of mature units. The plasmablasts were few in number during the whole of the period and the same applied to the multi-nuclear elements. Qualitative changes similar in nature to those noted in the previous case have also been observed a long time after the phosphorus treatment. In spite of the fact that the patient has relatively advanced skeletal changes, he has now, two years after the diagnosis was established and four years after the commencement of the disease, full bodily function and is practically free from pain.

Case 3. R. W. ♂ Aged 59. (Curves 5 and 6.) Autumn 1949, patient felt extremely tired and had diffuse pain. An examination in March 1950 revealed anaemia, a high S. R. (65) and a large amount of albumen in the urine. A roentgenological examination of the skeleton showed no signs of bone destruction. An examination of the blood produced the following result: Hb 52 %, Red cells 3,000,000, White cells 5,900 [Neutro: unsegm. 5, segm. 50, Eosin. 2, Bas. 1, Lymp. 21, Monocy. 10, Plasma cellular elem. 8 %].

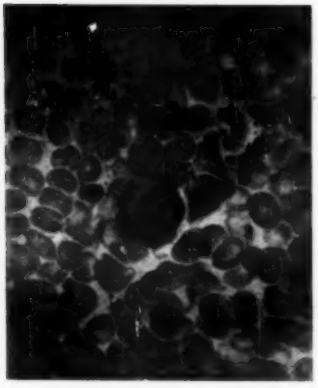


Fig. 6. (Case 3. Magn. × 560.) Smear preparation. Myeloma cell after treatment. Broken-up chromatin structure and irregular nucleolus.

Sternal puncture: Smear preparation: Normal marrow structure completely obliterated. The picture is dominated by plasma cell elements which make up about 50 % of the total cells. They are immature to half mature, have giant nuclei, and present appearances of malignancy. Myelopoiesis shows hypersegmentation and vacuolisation. Erythropoiesis is also toxically affected and of normoblastic type. Few megakaryocytes present. Reticulum unchanged. Plasma cell elements again found in the circulatory blood. Histological preparation: Marked increase of immature plasma cell elements.

In spite of the fact that the case, which could be one of myelomatosis or plasma cell leukaemia, was of an extremely pernicious type, phosphorus treatment was undertaken. It produced a certain alleviation of pain and a progressive decrease in the

plasma cell elements in the blood but no other changes were observed, excepting that the S. R. fell. Upon admission, the patient had no increase in the non protein nitrogen.

The patient's renal function, however, became much worse, he grew increasingly emaciated and died of uraemia after being eight months under observation. Morbid specimens obtained revealed bronchiectasis, infiltration of the liver, gross renal changes, a tumour in a rib, and a gelatinous myelomatous change in the stomach. An examination of the bone marrow carried out in this case showed no quantitative changes after the phosphorus treatment and towards the termination of the illness the number of malignant blastocytes increased. The changes found in the circulatory blood thus had no counterpart changes in the marrow cells, a fact which may probably be explained by the infiltration of the liver as shown post-mortem. Qualitative changes could, however, also be observed in this case after the phosphorus treatment and consisted of the breaking down and disintegration of the chromatin structure, the appearance of irregular nucleoli together with irregular vacuolisation in the cytoplasm of a number of the cells.

Case 4. O. S. ♂ Aged 72. The diagnosis of myelomatosis had been made three years previously, in 1947, and the patient treated with repeated blood transfusions. In Jan. 1949 he had severe systemic pain, a high degree of anaemia (haemoglobin 37 %), S. R. 163, total albumen 8.1 and globulin 5.3. Roentgen examination showed diffuse areas of destruction in the skeleton. In May 1950, the status was mainly unaltered, but the areas of destruction in the bones had considerably increased and the pain had become worse. *Bone marrow examination* at that time: Smear preparation: Ordinary cell count. The picture dominated by plasma cell elements which made up about 60 % of all the cells. They were chiefly immature and half-mature and at the same time exhibited conspicuously large nuclecli. Some of the cells showed strongly vacuolised, »out-seeping», protoplasm. Myelopoiesis without special characteristics. Hypoplastic erythropoiesis of normoblastic type.

In spite of the patient's poor condition, phosphorus treatment was commenced, and a short time afterwards the patient became free from pain. *Further examinations of the bone marrow* showed a decrease in the plasma cell elements. The total number of myeloma cells present in the bone marrow had fallen to 40 %, whereas on the occasions of the earlier examinations they had remained fairly constant around 60 %. The plasmablasts and multi-nuclear cells in particular had decreased in number, the former from 18.7 % to 7.7 %, and the latter from 5.4 % to 0.8 %. Furthermore, qualitative changes of the same type as in Case 3 had appeared. It was especially apparent that the vacuoles, previously rounded in shape, were now extremely irregular. No special effect upon the previously low trombocyte count could be observed, but at the same time the patient's tendency to bleed increased after the phosphorus treatment. The haemoglobin and the white cells were unaffected.

Discussion and Conclusions

In spite of the fact that the series of cases is a small one and to some extent has not been the subject of detailed observation, it permits in our opinion certain conclusions to be made. As regards the patient's symptoms, phosphorus treatment has caused a rapidly occurring alleviation of pain in every case, even where there has been diffuse processes

of destruction in the bony skeleton. The pain has completely disappeared in certain instances. This effect has been sustained. Pain was entirely absent for about four months in one case after phosphorus treatment. Quite apart from the method of treatment in itself, it is not associated with any kind of discomfort for the patient. Such secondary effects as nausea and indisposition which may occur for example after roentgen treatment have not been recorded after this form of irradiation. Treatment with *Urethane* effects the patient to a much more marked degree and is often very trying. Reactions during *Urethane* treatment may be so severe as to render its completion impossible or at least very difficult. Treatment with phosphorus is on the other hand, from this point of view, considerably superior. Lassitude, which is often a feature of this disease and which can often be most troublesome to the patient, has decreased in every case. In case 2, the feeling of tiredness completely disappeared and the patient was able to undertake relatively heavy work.

Demonstrable objective changes are seen above all in the bone marrow. The plasma cell elements decrease in number and particularly striking is a decrease in the number of immature and multi-nuclear cells present. Before these quantitative changes are observed, changes of a qualitative nature appear. They take the form of bizarre, irregular nucleoli and altered chromatin structure. In some cases breaking up, in others aggregation of the chromatin bars with disintegration of the nuclei and the appearance of large irregular vacuoles in the cytoplasm has been observed. After phosphorus doses in the order of 2—3 mC, such quantitative and qualitative changes have been recorded for periods of several months. Alterations in the circulatory blood in the form of a decrease in the number of plasma cell elements have also been noted; these were particularly obvious in Case 3. No signs of damage to the bone marrow in the form of an accentuation in the degree of anaemia, granulocytopenia or thrombocytopenia have been seen in any of the cases treated with phosphorus. A very definite tendency of the S. R. to fall has been observed. The blood albumen and the albumen content in the urine have not altered but detailed observations in these directions have not been carried out. The processes of bone destruction in the skeleton have not been affected by the phosphorus treatment and, moreover, it has done nothing to retard their progress. The very nature of the small amount of material permits of no conclusion as to whether or not the lives of the patients have been prolonged. The distinct changes produced in the bone marrow by radioactive phosphorus in the doses used are perhaps most interesting from a theoretical point of view, and are of such a nature and degree that it is our intention to continue the investigations already begun. It is conceivable that with a variation in the dosage, cell changes of a greater magnitude may occur and be longer sustained. In this connection it seems

to us that increased amounts of phosphorus ought to be tried, maybe in association with an alteration in the time intervals between the treatments. The results, as far as the patient's subjective condition is concerned, obtained with this form of treatment seem to us to be so encouraging that a continuation of the treatment of multiple myeloma with radioactive phosphorus appears to be justified.

SUMMARY

The authors discuss the results of the treatment of four cases of myelomatosis with radioactive phosphorus. The patients' subjective conditions were markedly improved. Certain alterations in the bone marrow were among the objective changes noted.

ZUSAMMENFASSUNG

Die Verfasser besprechen die Ergebnisse bei der Behandlung der Myelomatosis mit radio-aktivem Phosphor in 4 Fällen. Der subjektive Zustand der Patienten besserte sich merklich. Gewisse Veränderungen des Knochenmarks wurden festgestellt.

RÉSUMÉ

Les auteurs discutent les résultats du traitement de quatre cas de myélomatose par le phosphore radioactif. Les malades se sont sentis considérablement mieux. Parmi les signes objectifs on a relevé certains changements dans la composition de la moelle osseuse.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: PROFESSOR ÅKE ÅKERLUND),
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AN APPARATUS FOR COPYING OF ROENTGENOGRAMS[1]

by

K. Lindblom

Roentgenograms often have too great differences in translucency to be copied without some equalization. This may be done by two main methods: by directing extra light on the dark spots or by diminishing the light in the more translucent parts.

If the latter method be chosen, a paper of an adequate shape may be held in front of the translucent parts of the film, or an unsharp copy of the roentgenogram made and used as a filter (SPIEGLER & JURIS, FRANTZELL, MATTSSON). The former method has the disadvantages of causing overlapping of diffuse light on the picture; the latter consumes time and photographic material and may cause false reliefs where great contrast is present.

The author has constructed an apparatus for equalization of the translucency by increasing the light on the dark spots.

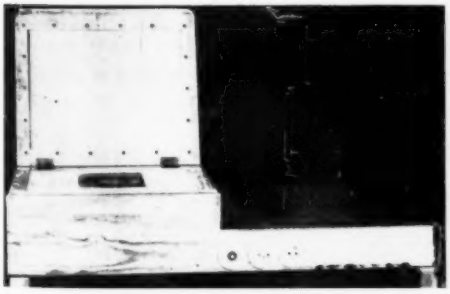

Fig. 1.

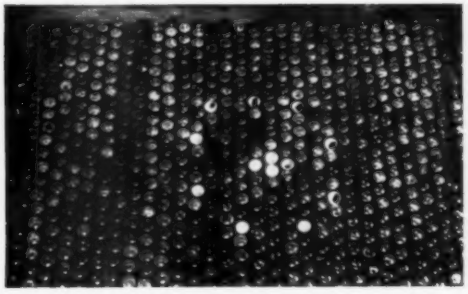

Fig. 2.

[1] Submitted for publication, March 15, 1951.

Fig. 3 a.

Fig. 3 b.

Twelve years ago, at the commencement of the experiments, about ten ordinary flashlight bulbs were used as a source of light. They were placed at a suitable distance behind the film. Seven years ago a more ambitious apparatus containing 294 flashlight bulbs in an area of 35 × 47 cm was built.

A new model of the apparatus[1] has recently been completed (Fig. 1); the number of bulbs is 704 in an area of 35 × 45 cm (Fig. 2). The film is placed on a cryolite glass, the bulbs lying under the dark spots are illuminated and the former raised or lowered so as to give an equal distribution of light over the film. The copy is made by contact or with a camera.

The effect of the equalization is illustrated in Fig. 3 a—b.

[1] Built by Mr. Pettersson, Roentgen Department, Karolinska Sjukhuset, Stockholm.

SUMMARY

Description of a new apparatus for copying of roentgenograms.

ZUSAMMENFASSUNG

Beschreibung eines neuen Apparates für Copierung von Röntgenbildern.

RÉSUMÉ

Description d'un nouvel appareil pour copier des roentgenogrammes.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR: DOCENT GUNNAR JÖNSSON),
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PERCUTANEOUS RETROGRADE PHLEBOGRAPHY OF THE LEG[1]

by

Tore Sylwan

According to the generally accepted technique, phlebography of the leg is carried out by injecting 10—20 cc of an aqueous solution of a contrast medium into a peripheral vein and taking films proximal to the site of such injection. It is possible by this method to show that the deep veins are permeable. But this, at present, is the only definite conclusion that can be drawn from this kind of phlebography, which may be suitably termed *centripetal* phlebography. LINDBLOM pointed out that there are several reasons for misinterpreting such phlebograms, especially if the leg be examinated in the horizontal position. The most important factor in this respect is probably the rapid sedimentation of the injected contrast solution, due to its relatively high specific gravity. Although the contrast medium may not fill a certain part of the venous system, it is not necessarily impossible for the blood to pass through it.

It should be mentioned here that in centripetal phlebography certain errors may be avoided by the injection of large quantities of the contrast medium. We have since 1947 in this department given injections of 40 cc of 35 % Umbradil solution. Other technical details of centripetal phlebography will not be dealt with in this report. In chronic venous disease of the leg the technique should be worked out individually after thorough clinical examination. Phlebography in the vertical position may, for instance, have to be supplemented by a radiological examination in the horizontal position, *e. g.* in cases of very marked varices.

[1] The main contents of this paper was read at the Meeting of the Swedish Surgical Association on Nov. 26, 1949; submitted for publication, Dec. 15, 1950.

The pictures obtained in centripetal phlebography may sometimes suggest that the deep veins are not easily permeable; but by reason of the many unknown and complicated factors that influence the venous circulation, the function of the deep veins cannot be assessed with certainty. The most we can say — even in cases where we obtain no filling at all of the deep veins — is that there may be something wrong with those vessels.

Yet, it is now fairly generally realized that a knowledge of the degree of permeability is not in itself the most important item required in the planning of treatment, and particularly surgical intervention, of chronic venous disease of the leg. The chief question is whether or not the deep veins are capable of receiving and transporting the blood flow from an area from which veins have been extirpated. On the other hand, there may be deep veins whose function is so defective that they simply cause extra strain on the remainder of the venous circulation.

BAUER used a special method of examining the function of the femoral vein by means of phlebography in order to investigate the problem. It was published in October 1948. In the operation BAUER injected iodine in aqueous solution through the exposed long saphenous vein into the proximal part of the femoral vein. The foot of the operating table was lowered to an angle of 45°. He obtained contrast filling of the femoro-popliteal vein in a great number of cases — in some instances as far down as into the tibial veins — in a film taken 1 minute after the injection. BAUER claims to have demonstrated insufficiency of the valves of the femoral vein in these cases as the contrast solution must have travelled downwards in a retrograde direction against the normal blood flow.

We have, for many years, been aware of the limitations of centripetal phlebography. We have considered the idea of using the rapid sedimentation of the contrast solution, as did BAUER, in an attempt to study the deep veins and their valves.

It is certainly an advantage to carry out retrograde phlebography in the Roentgen department by percutaneous injection. It is then possible *before* operation to ascertain whether surgical intervention is indeed indicated, and if so, to devise the most suitable operative technique. The technical resources of the Roentgen department may be utilized and the problem of having to consider asepsis in the operation theatre is eliminated.

During the year April 1, 1949—April 1, 1950, I carried out a total of 96 retrograde phlebograms with percutaneous injection of contrast medium into the femoral vein. A great number of these were supplemented by other phlebographic examinations, different centripetal forms as well as special examinations in collaboration with Dr. SEVED NEIJ

of the Surgical Department I of this Hospital. Most of the latter were carried out during operations on the veins.

Technique

The following technique in percutaneous retrograde phlebography is employed.

The patient is placed in the supine position on a table with a foot support. The latter is lowered until the table forms an angle of 65° with the horizontal plane. The femoral vein is punctured immediately below the inguinal ligament, with a long needle of about 1 mm diameter, directed toward the knee. The procedure is as a rule fairly simple, as this part of the vein runs along the medial side of the artery, the pulsation of which can be felt. 40 cc of a 35 % Umbradil solution are injected in two parts — firstly 20 cc very slowly over a period of about 1 minute. At the middle of this injection phase and again at its close, films of the thigh are taken in the sagittal plane. A further 20 cc are then injected as quickly as possible. Towards the end of this second phase a third sagittal film of the thigh is taken and then, immediately after the injection, films of the thigh, the knee and the calf are taken in sagittal and lateral planes.

In all, I usually take six to seven films in the course of 3—4 minutes. All the films are obtained with the tube tilted 10° to 12° towards the feet. The focus-film distance is 1 metre. The exposure period need not be particularly short — $^1/_2$ to 1 second at about 70 kV. It is advisable, at least for the films of the thigh, to use a secondary diaphragm.

Discussion of Results

The purpose of one slow and one quick injection is seen in fig. 1. If there be a slowly ascending blood flow in the femoral vein, it will keep the valves slightly open so that the descending contrast solution can travel down between them (fig. 1 a). During the second injection phase (fig. 1 b) there is a maximum rise in the injection pressure and the valves are pressed together so that the bulk of the contrast solution travels upwards. In fig. 2 the opposite has occurred. With a forced injection (fig. 2 b) the density of the medium increases distally in the vein. The valvular sinuses are not so clearly outlined and regular as in fig. 1.

In my opinion functional insufficiency of a deep vein may be postulated only in cases similar to the one in fig. 2. The phlebograms must be assessed, however, with caution in such cases. The contrast medium at times runs down the long saphenous vein, as far as to outline the

Fig. 1 a. Fig. 1 b.

Fig. 1. Retrograde flow of contrast solution despite sufficient valves.

a. Slow injection. The medium, injected above the proximal valves, fills the whole of the superficial femoral vein. This film was taken when nearly 20 cc had been injected, and during the injection.

b. Forced injection. The film was taken 1/2 minute later than 1 a, during the rapid injection of another 20 cc of the contrast solution. There is very dense contrast in the femoral vein above the proximal valves which apparently have closed. Below these valves is less contrast in the superficial femoral vein than during the slow injection, the density decreasing distally.

The marked sedimentation of contrast substance in the valvular sinuses — which is probably a sign of sufficiency of the valves — is commonly seen in retrograde phlebography.

subcutaneous veins of the calf, as seen in fig. 3. The superficial femoral vein will then fill rapidly with dense contrast fluid which has passed up the vein from below via the communicating vessels from the superficial veins. Fig. 3 c was taken slightly more than 1 minute after the beginning of the injection. In this case there is no evidence of insufficiency of the valves in the femoral vein.

Some »normal cases» were examined in connection with urography. Young persons were selected, the oldest being 22 years of age, with legs subjectively and objectively free from signs; the women were 0-paras. Step-like filling of the deep veins, of the same type as fig. 1, was obtained in one of these cases. The contrast medium was arrested in the remainder at the proximal pair of valves and travelled only proximally in the common femoral vein. Although only four such examinations were made, the results may support the theory that a retrograde flow, as fig. 2, may be due to pathological changes in the deep veins. Further evidence in favour of this opinion was obtained by the examination of both legs of a 42 years old man who had suffered for several years with progressive cramps and sensations of heaviness in the right leg. He had no visible varices or skin lesions. There was a slight rise in the temperature of the skin of the right leg only. The left leg was subjectively and objectively free from signs. Clinical examination of the arteries and arteriography gave negative results.

Fig. 2 a. Fig. 2 b. Fig. 2 c.

Fig. 2. Retrograde flow of contrast medium in supposed valvular insufficiency.

a. Slow injection. There is contrast substance in the superficial femoral vein and the visible part of the popliteal vein.

b. Forced injection. Larger amounts of contrast medium in the femoral and popliteal vein, the density increasing successively in the distal parts. No sedimentation in the valvular sinuses is seen in the vein stems.

c. The subcutaneous veins of the calf are filled 3 minutes after the beginning of the injection. *During* the injection no contrast medium was seen in the subcutaneous veins above the popliteal fossa. The contrast substance has thus travelled in an abnormal direction from the deep to the superficial veins.

Centripetal phlebography demonstrated free passage through the deep veins. Fig. 4 shows the results of the retrograde phlebography of both legs.

The value of retrograde phlebography as evidence of the *function*

Fig. 3 a. Fig. 3 b. Fig. 3 c.

Fig. 3. The importance of taking films *during* the injection to avoid errors.

a. 1/2 minute after the beginning of the slow injection nearly all of the opaque medium is seen to travel down into the long saphenous vein. Only the proximal part of the femoral vein contains a small amount of the medium.

b. Less than 1 1/2 minute after the beginning of the injection there is dense contrast filling of the whole of the femoral vein.

c. A film of the lower leg shows that the contrast substance has entered the deep veins from the subcutaneous branches. In this case the femoral vein has filled from below. The examination gives no information concerning the function of the deep veins.

of the deep veins is, in spite of this, doubtful. As the physiology of the venous circulation in the legs is still not completely understood results like those reported here cannot be absolutely reliable, in so far as they be taken as a measure of the capacity of the veins to transport the blood away from the legs. *Anatomically*, however, many of the examinations revealed pathologic changes in the deep veins of the thigh, which in some regards were of a remarkable nature.

In fig. 5 there is no trace of the contrast substance in the superficial femoral vein, nor in the long saphenous vein. It is the profunda femoris vein that occupies the thigh with its dilated, varicose branches. This

Fig. 4 a. Fig. 4 b.

Fig. 4. Retrograde phlebography of a patient with one »diseased» and one »healthy» leg.

a. Right leg. Clinical symptoms of deep venous insufficiency (see text). Retrograde filling of the superficial femoral and the upper part of the popliteal vein with no sedimentation in the valvular sinuses. The profunda femoris vein is also filled, and, judging from the other films of this examination, this filling partly occurred in a retrograde direction.

b. Left leg. No subjective or objective signs. The contrast solution travelled only as far down as seen in this film, both with slow and with quick injection.

is not the true anatomical appearance of the deep femoral vein. Fig. 5 b was taken 30 seconds after fig. 5 a and shows indirectly that this vein must have a wide communication with the superficial varicose veins of the calf.

In fig. 6 the varicous nature of the distal branches of the profunda femoris vein are more clearly distinguishable. The contrast solution runs straight down from this deep vein into the short saphenous vein through a communicating vessel, 8 mm in width, which has no valves. The popliteal and the superficial femoral veins fill from below through the short saphenous vein and not, like the profunda femoris, in a retrograde direction from above.

Fig. 7 shows a further case in which retrograde filling of the deep femoral vein was obtained. There are wide communications which in this case appear to be connected with the long saphenous vein in the popliteal fossa. As a result of such a wide communication the load on the flow of blood from the veins of the lower leg must be considerable. There is also evidence of retrograde filling of the superficial femoral vein.

Retrograde filling of the *deep* femoral vein, suggesting valvular insufficiency, was noted in 28 examinations. The *superficial* femoral vein appeared to be insufficient in 27 examinations.

In all, there was suspected insufficiency of the deep veins of the thigh in 40 cases; in 15 cases the retrograde phlebograms showed signs of disturbed function of both veins simultaneously. In another 15 ex-

Fig. 5 a. Fig. 5 b.

Fig. 5. Pathological changes in the profunda femoris vein.

a. Only the profunda femoris vein was visualized in the thigh. There is very marked dilatation of all parts of the vein. No valvular sinuses are visible. Varicous changes are seen, particularly in the distal branches.

b. From the profunda femoris vein the contrast medium has travelled down into the superficial varices of the calf.

aminations the contrast medium passed downwards into the long saphenous vein or accessory subcutaneous veins of the thigh and an assessment of the function of the deep veins was not found to be possible.

In 11 cases a directly observable communication — or several — between the deep veins of the thigh and the superficial varices filled in a retrograde direction. In a further 14 cases a communication of this pathological type was demonstrated indirectly as in fig. 2.

Nearly all these communications were seen in the region of the hiatus adductorius. This situation has also been found to be the site of predilection of deep varices, affecting branches of the profunda femoris vein, communications between this vein and the superficial

Fig. 6 a. Fig. 6 b. Fig. 6 c. Fig. 6 d.

Fig. 6. Visualization of abnormal communication from the profunda femoris vein to the short saphenous vein.

a. Slow injection. About 50 seconds after the injection was started, there is dense contrast filling of the profunda femoris vein. The branches of this vein are wide and varicose, especially the distal ones. A very small amount of the opaque medium is seen in the superficial femoral vein. It has probably passed therein through small communicating vessels from the profunda femoris (arrow); in a film 30 seconds earlier there is no contrast filling of the superficial femoral vein though the profunda femoris is somewhat densely filled.

b. 1 minute after the forced injection was ended and the cannula taken away, the superficial femoral vein is also filled with dense contrast.

c. In the lateral view the contrast solution is seen to pass straight down into the proximal end of the short saphenous vein through a communication from the profunda femoris vein. This communication, nearly 1 cm wide, is also seen in the frontal pictures but is overlapped by bone (arrow in fig. 6 b). From the proximal part of the short saphenous vein the superficial femoral vein is filled in a centripetal direction.

d. The contrast medium has travelled far down into the branches of the short saphenous vein.

femoral vein, or the vessels which connect the superficial and deep veins. Varicose lesions of this type were seen in 41 examinations, including those with retrograde filling of subcutaneous veins.

The typical localization of the deep varices is seen in fig. 8. Varices of this kind cannot be demonstrated with clinical certainty or by means of centripetal phlebography. The same applies to pathologic communicating veins in the thigh, which are probably not rare phenomena.

Fig. 7. Fig. 8 a. Fig. 8 b.

Fig. 7. The usual localization of deep varices in the thigh is dorsal and distal to the site of the hiatus adductorius.

Fig. 8. Retrograde flow of contrast medium from the deep veins of the thigh to the long saphenous vein via communicating branches on the level with the hiatus adductorius.

a. Pathologic changes appear to be present in the superficial femoral vein as well as the profunda femoris vein. A network of communicating vessels is filled retrogradely from both these veins.

b. The contrast medium has passed into the superficial varices of the calf and above the knee.

Percutaneous retrograde phlebography gives valuable information concerning the deep veins which cannot be obtained with any other method of examination. The results, however, are limited to the veins

Fig. 9 a. Fig. 9 b. Fig. 9 c.

Fig. 9. Retrograde phlebography with percutaneous puncture of the popliteal vein.

a. 20 cc of 35 % Umbradil solution were injected during a period of 20 seconds. This film was taken at the end of the injection — the cannula is seen at the top of the picture. The opaque medium has travelled far down into the deep veins of the calf, in which there are numerous regularly shaped valvular sinuses. It is not possible to assess the venous function from this film.

b. No further injection was made. In a film taken 1/2 minute later than a. there is less contrast filling of the deep veins and a good deal of the opaque medium is seen in the short saphenous vein.

c. After a few muscular contractions the contrast medium has entered numerous varicose superficial branches. This suggests the presence of pathologic changes in the communicating veins of the lower leg.

of the thigh. The deep veins below the knee are not accessible when the contrast medium is injected into the proximal part of the femoral vein. Retrograde filling of the tibio-fibolar veins was obtained in no instance in the present series. When these veins were outlined the subcutaneous veins were simultaneously or previously seen to be filled with the medium.

In those cases where the retrograde flow of the medium is arrested by the proximal valves in the femoral veins, it is impossible to state with certainty that pathologic changes have not occurred more distally.

Fig. 10. Retrograde phlebography in occlusion of the femoral vein.

a. No valves are seen in the narrow vicarious vessels in the thigh which appear to consist partly of dilated vasa vasorum.
b. The contrast solution has travelled straight down into the short saphenous vein.

Fig. 10 a. Fig. 10 b.

Because of such shortcomings of the method I have tried to carry out retrograde phlebography by injecting the contrast medium into the popliteal vein (fig. 9). The puncture of the vein in the popliteal fossa was found to be easier than had been expected. It was, however, difficult to keep the needle in the vein after the injection was commenced. The method was abandoned after 12 examinations, of which six were unsuccessful by reason of extravasal injections.

Retrograde phlebography of the femoral veins is indicated in chronic venous disease of the legs when there is reason to suspect pathologic changes in the deep veins, and the possibilities of surgical treatment have to be examined. It is particularly important to make this examination before those operations of the superficial femoral and the popliteal vein which are performed nowadays. After extirpation of the superficial femoral vein the deep femoral vein has to convey most of the blood

flow away from the lower limb. It is clear from the investigation that the deep femoral vein is itself often the seat of pathologic changes. It should also be noticed that abnormal communications like those described in the foregoing, are no doubt a common cause of relapsing varices after ligation or extirpation of the superficial venous trunks.

The examination is not indicated in acute deep thrombosis. It is contraindicated in my opinion in severe affections of the kidneys and the liver, in severe heart disease with loss of compensation, and in cases of hypersensitivity to the contrast medium. In every case a test was made with an intravenous injection of 1 cc of Umbradil solution, at least 1 hour prior to the examination.

Of the 96 examinations in which the femoral vein was punctured, 9 were complete failures, in most instances because the patient fainted. In two or three cases it was found impossible to puncture the vein, probably due to obliteration of the femoral vein. Puncture of the vicarious vessels may be extremely difficult, if they are as narrow as in fig. 10. The picture seen here has been described by BAUER, in his work on retrograde phlebography, as being produced by dilatation of the vasa vasorum in the wall of the obliterated vein. In such cases retrograde phlebography should be carried out after exposure of the vein.

The tendency to faint during the examination is a common phenomenon. It may be counteracted by premedication in the same manner as before operation. I avoided this, however, as nearly all the patients in my series were ambulant at the time of examination. The risks involved are small. In two cases of marked obesity extravasal injection produced phlegmonous lesions of the subcutaneous tissue and caused the patients great inconvenience. Thrombosis as a sequel of the examination was not seen in any of the cases. None of the patients received anticoagulants in any form. They were simply told to be up and about as usual and to come to the hospital immediately in the event of symptoms arising.

The method, as described above, has some technical disadvantages. The relatively short film size — 40 cm — which has to be used, provides an unsatisfactory survey of the vessels. There is at times insufficient time to change the cassettes or to readjust the tubes quickly enough. Vascular lesions may therefore be missed, because the contrast medium has left some important vessels before the film is taken. Elaborate and expensive technical resources would be required to eliminate these drawbacks. With the technique described retrograde phlebography may be carried out in most roentgen departments by fairly simple means, and it is no more complicated than centripetal phlebography of the ordinary variety.

Conclusions

Pathological changes in the deep veins of the thigh may be shown by means of retrograde phlebography. This is not possible by any other method of investigation. The essentials required in order that an opinion may be formed upon the result of such an examination are: — that films of the leg be obtained in at least two right-angled projections; that films be made really early as the injection of the contrast medium is being carried out; that films both of the thigh and the calf be taken. These essentials can scarcely be obtained if the contrast medium be injected into a vessel exposed upon the operation table.

96 retrograde phlebographs have been carried out with percutaneous injections of a contrast medium into the upper part of the vena femoralis. The technique which has been elaborated is simple and may be performed in any roentgen department. The following observations have been made: a. Pathological changes in the deep veins of the thigh appear to be common in chronic venous diseases. b. Changes have been encountered in the vena profunda femoris at least as often as in the vena femoralis. c. The presence of pathological communications with a retrograde direction of flow from the deep to the outer veins of the thigh have been established in addition to the common occurrence of deep varicosities. d. The site of predilection for anatomical changes is the region around the hiatus adductorius.

SUMMARY

Following an appreciation of the limitations of centripetal phlebography, the technique of percutaneous retrograde phlebography is described in detail. The results observed in 96 cases examined by the latter method are discussed and the advantages of the method are pointed out.

ZUSAMMENFASSUNG

Im Anschluss an einer kritischen Betrachtung der Grenzen bei der centripetalen Phlebographie wird die Technik der perkutanen retrograden Phlebographie in ihren Einzelheiten beschrieben. Die beobachteten Ergebnisse bei 96 mit dieser Methode untersuchten Fälle werden besprochen, wobei auf die Vorteile dieser Methode aufmerksam gemacht wird.

RÉSUMÉ

Après une évaluation des limites de la phlébographie centripétale, l'auteur décrit la technique détaillée de la phlébographie percutanée. Les résultats observés dans 96 cas examinés par cette dernière méthode sont discutés, et les avantages de la méthode sont signalés.

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FROM THE ROENTGEN DEPARTMENT (DIRECTOR AT THE TIME OF THE INVESTIGATION: DR. M. SIMON) OF SABBATSBERGS SJUKHUS, STOCKHOLM, SWEDEN

A PHLEBOGRAPHIC STUDY OF CONSTRICTIVE PROCESSES IN THE SUPERIOR VENA CAVA AREA AND OF ACCOMPANYING CHANGES IN THE COLLATERAL CIRCULATION[1]

by

Ernst F. Salén

The symptomatology in occlusion of the superior vena cava has been known since the beginning of the 19th century, when this anomaly was described by the Frenchman CORVISART (1806). The clinical picture is well known, its main features being stasis in the veins of the neck, arms and thorax and the development of a collateral circulation within these vessel paths. In some cases, the clinical picture is not characteristic. It is then important to make an exact determination of the degree of stenosis and an estimation of the course of the collateral circulation. Mediastinal phlebography (angiocardiography) in perpendicular planes is valuable in such cases.

Mediastinal phlebography with exposures in *one* plane only in lesions of the superior vena cava has been described by, amongst others, the Mount Sinai group with SUSSMAN & GRISHMAN and in Sweden by LINDBLOM.

Mediastinal phlebography according to the first-mentioned method with simultaneous roentgenology in perpendicular planes has been performed by the writer in 27 cases of varying degrees of stenosis of the superior vena cava. Constrictions giving rise to a collateral circulation were considered to be severe. All the cases of intrathoracic tumours with stenosis of the vena cava and collateral circulation consisted of mediastinal metastases from inoperable tumours of the lung. Severe stenosis of the vena cava was also found in cases of postoperative

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thrombophlebitis and as a result of systemic diseases such as Hodgkin's disease (lymphogranulomatosis) and lymphosarcoma (see table).

No. of phlebographies (in two planes) in stenosis of the superior vena cava area = 27

	Intrathoracic tumours	Thrombo-phlebitis	Systemic diseases
With collateral circulation	5	3	1
No collateral circulation	14	2	2

The question then arises which venous paths may supply the superior vena cava area when this region is blocked. Two different venous systems function as substitute paths. One consists of the various groups of superficial veins which have their course in the thoracic wall. The other is a system of deep veins, the azygos system, which runs in the posterior portion of the abdominal cavity up through the posterior mediastinum. The internal mammary veins, which run paired on the inner side of the anterior thoracic wall and which connect caudally with the veins in the anterior abdominal wall — which, in turn, anastomose with the inferior vena cava system — belong to the group of superficial veins. The internal mammary veins open cranially into the innominate veins. Communication is established in the same way through the lateral thoracic veins, which run bilaterally in the thorax and connect caudally with the venous system of the abdominal wall. This, in turn, empties into the inferior vena cava system. Cranially, the lateral thoracic veins open into the left and right axillary veins, respectively. In the posterior superior portion of the abdominal cavity, the azygos vein originates and has its course in the posterior part of the mediastinum, immediately anterior to the right part of the thoracic spinal column. At the level of the right lung hilus it arches forward over the right main bronchus and opens into the posterior wall of the superior vena cava immediately before the latter vessel pierces the pericardium. In the terminal segment its calibre is approximately five millimeters.

From the superior posterior part of the mediastinum, the azygos vein receives the supreme intercostal vein, which runs in the same direction, and which collects the blood from the uppermost intercostal veins. In the abdominal cavity, the azygos is connected with the inferior vena cava *via* the upper lumbar veins. This also applies to the hemiazygos vein — of considerably smaller calibre — which runs mainly parallel to the azygos, somewhat to the left of the midline, and opens into the azygos vein in the lower part of the thoracic cavity.

Fig. 1. Case 2. Phlebogram showing marked stenosis in the superior vena cava and a reversed contrast flow in the azygos vein.

Finally, the forementioned venous stems, running mainly in a longitudinal direction, are connected with each other through the transvere intercostal veins. Thus, there are a number of substitute paths which are able to replace the venous return circulation in various forms of blocking of the superior vena cava area. This is illustrated by the following typical cases.

Case 1. E. O. L. G., aged 27. K 1 4206/48.

The patient was a railway employee, sent to the department of thoracic surgery with a diagnosis of right-sided bronchial carcinoma confirmed by a biopsy specimen taken on bronchoscopy. Slight stasis in the thoracic and cervical veins, indicating an obstruction in the superior vena cava area, was found on clinical examination. Phlebography in two perpendicular planes showed a marked stenosis of the superior vena cava, inferior to the insertion of the azygos vein, whose arched terminal segment was contrast-filled in a reversed direction. (Fig. 1.)

Case 2. G. H. F., aged 46. K 1 22/49.

The patient was a married woman, sent to the department of thoracic surgery for further investigation of stenosis of the superior vena cava of unknown origin. Since 1944, she had noticed oedema, severe even at rest, in the upper part of the body, particularly in the face, hands and arms. Active movements increased the oedema and her lips became slightly blue. She had no headache.

An obstruction in the superior vena cava, approximately 4 cm above the right auricle, was found on attempted catheterization of the heart. The venous pressure at this point was 22 cm of water.

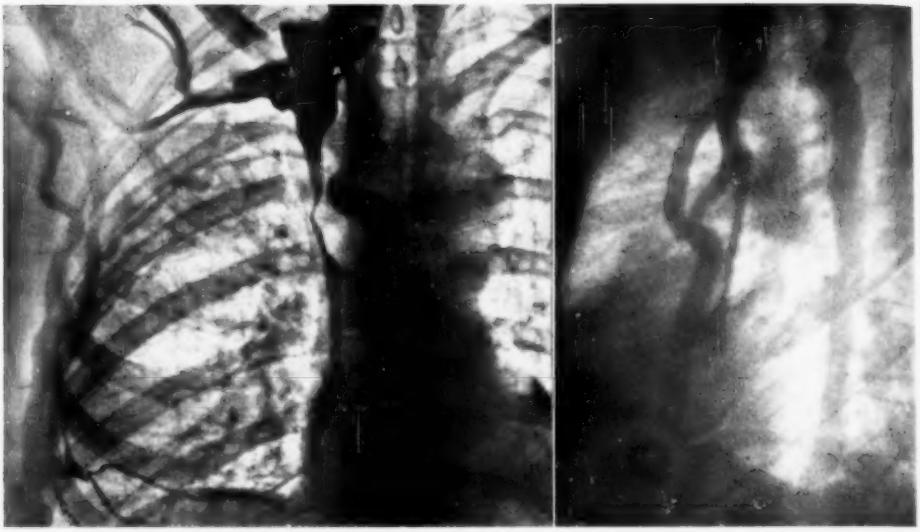

Fig. 2 a. Fig. 2 b.

Fig. 2. Case 2. Phlebogram showing extensive stenosis of the superior vena cava at the insertion of the azygos vein. There was also a collateral circulation in the superficial thoracic veins with a reversed contrast-flow in the azygos vein.

Phlebography made in two planes (Fig. 2) showed extensive stenosis of the superior vena cava. The terminal segment of the azygos vein was also involved. In order to establish the central limits of the stenosis more clearly, *retrograde phlebography* was also carried out. A catheter was then passed through the great saphenous vein, the inferior vena cava and through the right auricle until the tip of the catheter reached the central portion of the stenosis (see Fig. 3). The contrast medium was injected with a special high pressure syringe (according to JÖNSSON). It was thus possible to localize the central limits of the stenosis to the level of the right branch of the pulmonary artery. Its length was approximately 5 cm. The origin was uncertain, but the stenosis had presumably arisen through chronic inflammation. Since the symptoms became somewhat less severe, the patient was discharged from hospital but was kept under observation.

Case 3. B. F. B., aged 48. K 1 1944/48.

The patient was a manual worker. He was sent to the department of thoracic surgery for a dermoid cyst, the size of a human head, on the right side of the mediastinum. On operation, the tumour was found to be attached to the left innominate vein at the insertion of the superior vena cava. As the mass was dissected out from this site, there was a sudden severe haemorrhage from the posterior side of the superior vena cava at the insertion of the left innominate vein, which was almost completely severed from the vena cava. The ruptures in the vena cava and the innominate vein were sutured with fine silk.

Fig. 3. Case 2. Retrograde phlebogram showing central limits of the stenosis.

Fig. 4. Case 3. Phlebogram (injection in left cubital vein) showing obliteration of central segment of left innominate vein.

Approximately one week after the operation, the left arm and shoulder became very swollen. As thrombosis was suspected, heparin was administered. After 10 days the swelling started to subside and 2 1/2 months after the operation the arm was entirely free from swelling. Control by means of *phlebography* with injection in the *right* cubital vein showed normal passage through the right innominate vein and the superior vena cava. *Phlebography* from the *left* side showed obliteration of the central segment of the left innominate vein. The contrast medium had passed through collateral veins over to the right innominate and the superior vena cava (see fig. 4).

Discussion

In stenosis of the superior vena cava, the venous backflow may — as described in the foregoing — take place in several ways. The azygos system therefore appears to be an important collateral path in man.

Experiments on dogs with ligature of the superior vena cava have shown, on the other hand, that the azygos system of these animals does not possess the same adaptability under altered circulatory conditions

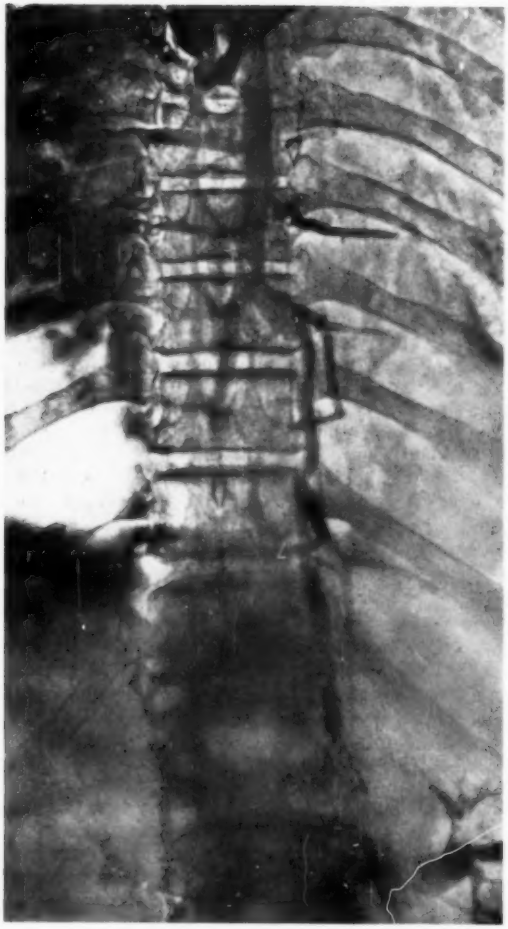

Fig. 5. Autopsy material. Contrast-filled azygos vein.

on injection of the contrast medium. In found to offer considerable resistance (see

as that of man (CARLSON 1934). These investigations have shown that an adequate venous return circulation occurs only when the ligature lies peripheral to the insertion of the azygos vein. If the terminal segment of the azygos is also ligated, this vein can only to a limited extent convey the blood stream to the heart in a reversed direction *via* the inferior vena cava. In man, on the contrary, the azygos system appears to become more easily adapted to a reversed circulation. The reason remains as yet unelucidated. It is possible that the anatomic difference in the structure of the valves may play some rôle. The valves in the terminal segment of the azygos would then become insufficient or would already be functionally insufficient under physiological conditions.

A few experiments have been made with injections on autopsy material. In some cases it was possible to fill the azygos veins in a reversed direction without any marked increase in pressure other cases the valves were Fig. 5).

SUMMARY

Simultaneous phlebography in two perpendicular planes was made in 27 cases of occlusion of the superior vena cava. In the majority of cases it was possible to determine the extent of the stenosis. In the other cases, complementary retrograde phlebography was performed by means of a heart catheter introduced from the great saphenous vein via the inferior vena cava and the right auricle.

The course of the collateral circulation was shown in 9 cases of severe stenosis. The azygos system provides the possibility of a collateral circulation between the superior vena cava and the inferior vena cava region in a reverse direction.

ZUSAMMENFASSUNG

Bei 27 Fällen mit einem Verschluss der Vena cava superior wurden gleichzeitig phlebograpische Aufnahmen in zwei auf einander senkrecht stehenden Ebenen vorgenommen. In der Mehrzahl der Fälle war es möglich, das Ausmass der Stenose zu bestimmen. In den anderen Fällen erfolgte als Ergänzung die retrograde Phlebographie mit Hilfe eines Herz-Katheters, der von der Vena saphena magna über die Vena cava inferior und die rechte Vorkammer eingeführt wurde.

Der Weg des Kollateral-Kreislaufs wurde in 9 Fällen schwerer Stenose ersichtlich. Das Azygos-System schafft die Möglichkeit eines Kollateral-Kreislaufes zwischen dem Versorgungs-Gebiet der Vena cava superior und der Vena cava inferior in umgekehrter Richtung.

RÉSUMÉ

Dans 27 cas d'occlusion de la veine cave supérieure il a été pratiqué des phlébographies simultanément dans deux plans perpendiculaires. Dans la majorité des cas il a été possible de déterminer les limites du rétrécissement. Dans les autres cas, une phlébographie complémentaire rétrograde a été opérée à l'aide d'une sonde introduite par la veine fémorale, la veine cave inférieure et l'oreillette droite.

Le parcours de la circulation collatérale est mis en évidence dans 9 cas de rétrécissement grave. Le système des veines azygos permet la circulation collatérale entre la région de la veine cave supérieure et la veine cave inférieure donc en sens opposé à la normale.

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